AN INVESTIGATION INTO THE NEURAL MECHANISMS OF HUMAN BALANCE CONTROL

by

TIMOTHY MARK OSBORNE

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University of Birmingham

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ABSTRACT

The mechanisms of neural control of human balance, and in particular upright stance, are still not fully understood. Most authors understand balance to be controlled through relatively simple reflex mechanisms, but some groups propose balance is dominated by higher level control.

I develop new semi-automatic techniques which can follow very small changes in muscle length via ultrasonography. I use this technique to uncover a high sensitivity control mechanism in human standing that is more consistent with reflex than higher level control. Further experiments suggest reflex control is present, albeit at a low gain, in a balance control task that is similar to standing, but that higher level control mechanisms dominate. A final investigation into visuo-manual balance suggests that control alternates between actions and sensation which facilitates higher quality sensory feedback.

I hypothesise that balance is maintained by parallel neural pathways. Reflex control operates at low gain to increase the time constant of the human inverted pendulum. This facilitates the operation of a higher level controller that is subject to longer time delays. I speculate that higher level serial ballistic control may enable higher quality feedback than would be possible otherwise.

DEDICATION

Dedicated to my parents John and Sally Osborne,

without whose unflinching support and gentle encouragement

this would not have been possible.

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Chapter 1

GENERAL INTRODUCTION

'Balance is the ability to maintain functional equilibrium' (Eckert, 1979: 149). For a physical entity this simply means the ability to remain upright and steady. An object or system can be balanced and stable or balanced and unstable. To discover whether a balanced object is stable or unstable requires a perturbation. If, when perturbed, the object falls over it is unstable. More technically, when an object is unstable the effect of even the smallest perturbation is to produce forces that increase the deviation away from the point of equilibrium. A stable object will not be knocked over by a perturbation: external forces will be counteracted by a restoring force that moves the object back towards its point of equilibrium.

Many inanimate objects are *passively* stable: they require no active intervention to keep them balanced. Tables, chairs, (and most forms of furniture!), are all examples of passively stable objects. Passive stability is normally advantageous - life would become rather difficult if household objects had a natural tendency to fall over. Some systems or objects are, however, passively unstable. In this case balance can only be achieved with some extra help. Passively instability is normally undesirable unless it serves some functional purpose. For example, when sat on a swiss exercise ball, the user is intentionally subjecting themselves to an unstable state. Maintaining balance in this situation is a form of exercise because of the constant corrective action required from postural muscles. Thus in this example the system (the swiss ball plus the person) is passively unstable, but is balanced by corrective actions

from the user. This may be contrasted with sitting in a rocking chair where external forces will cause the chair to rock back and forth but not to fall over because it is passively stable.

A variety of researchers are interested in how humans balance themselves while standing up. Engineers look to biology to inspire novel control paradigms (Bottaro *et al.*, 2008; Gawthrop *et al.*, 2011), medical professionals search for a greater understanding of balance disorders (Mergner, 2010), and biologists look at human bipedal stance from an evolutionary perspective (Schmitt, 2003). Human balance control is of particular interest. When standing, humans have a small base of support (the feet) and a high centre of mass (CoM). Bipedal stance does have major advantages. For example, standing on two legs frees the upper limbs for purposes other than balance such as the use of tools. However, upright stance also comes at a price. Lower back pain, the pooling of blood in the lower limbs leading to varicose veins, and other cardiovascular problems associated with a tall erect posture are well documented. Furthermore, balance in this position is rather precarious. Whether passively or actively balanced, a system will only maintain balance while the vertical location of the CoM does not exceed the limits of the base of support. Thus, in standing, the task is to keep the CoM location within a relatively small range provided by the feet. In reality this is complex because humans have many joints and muscles, and the study of such a process at first appears overwhelming. However, researchers have developed a useful simplification of the task which significantly reduces the complexity.

The inverted pendulum model and human control pathways

The majority of human sway proceeds as synchronous movements of all body parts in the sagittal plane around the axis of the ankle joints (Gatev *et al.*, 1999). Medial/lateral sway is

also present but is smaller than sagittal sway (Winter *et al.*, 1998). Gatev *et al* (1999) have used a multi-camera system to show that ankle mechanisms in the sagittal plane dominate quiet standing control. Consequently, the task of human balance can be reasonably simplified to the task of balancing a single axis inverted pendulum. Several studies have provided evidence to validate this model. Winter *et al.*, (1998) showed that body sway oscillations fit the equation of motion of an inverted pendulum. Numerous studies have demonstrated that subjects can easily balance a real inverted pendulum using ankle torques (Fitzpatrick & Taylor, 1992; Loram & Lakie, 2002*a*) even with greatly reduced sensory inputs (Fitzpatrick *et al.*, 1994). Despite its apparent simplicity, the inverted pendulum model can even be used to predict calf muscle length changes during quiet standing with remarkable precision (Loram *et al.*, 2005*a*). Thus, reducing human balance to the task of balancing an inverted pendulum is advantageous because it changes a highly complex task with a large number of variables to a simple one with fewer variables, whilst still capturing the essence of the task. How do we go about reducing the human body to such a simple object?

Figure 1 shows a schematic of the inverted pendulum model that is used throughout this thesis. The dynamics of the inverted pendulum depend on three factors: the mass of the pendulum (*m*), the height of the mass above the axis of rotation (*h*), and the force of gravity acting upon the pendulum (*g*). Within a fairly small range of angles relevant to human balance, the product of these variables (*mgh*) determines the toppling torque per unit angle of the inverted pendulum. This is the amount of torque per unit angle required to stop the pendulum from falling over. For example, to maintain the balance of an inverted pendulum with a mass of 70 kg and height of 1 m at a forward lean of 1 degree requires 11.97 Nm of

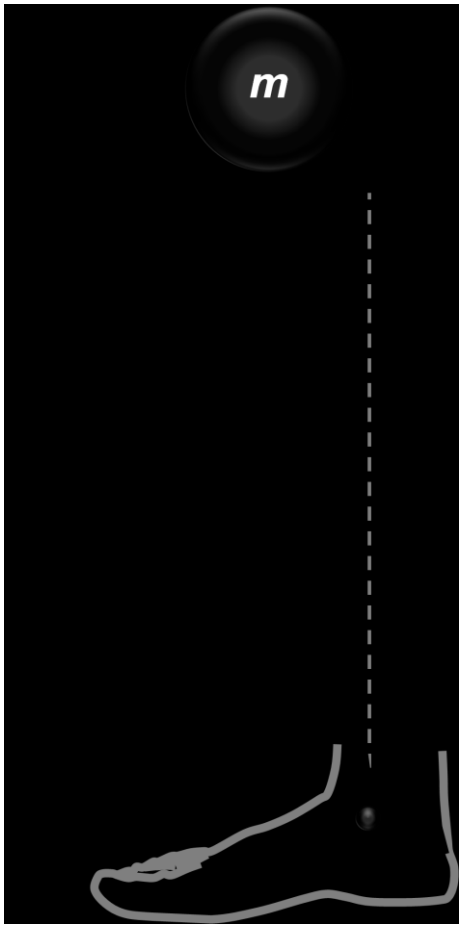

Figure 1. Inverted pendulum model of human standing.

The model consists of a mass (m) that rotates around the axis of the ankle joints in the sagittal plane.

torque. To maintain balance at a forward lean of 2 degrees would require twice this amount of torque (23.94 Nm). Thus, to prevent the 'human inverted pendulum' from falling over requires an adequate level of restoring torques. How are corrective torques produced in human balance?

Figure 2 depicts a simplified conception of human balance control. Three parallel pathways are available for producing torque (Loram *et al.*, 2009*c*). The inner (passive) loop concerns the intrinsic properties of the ankle joints such as stiffness and damping that provide an immediate (zero delay) torque response to unexpected disturbances. The middle (reflex) loop concerns neural reflex mechanisms that act continuously through the spinal cord, brain stem, cortex and cerebellum (Deliagina *et al.*, 2007). This loop is associated with a wide range of delays between 40 and up to 180 ms depending on the level of complexity of the reflex and the intensity of the stimulus (Horak *et al.*, 1997). Finally, the outer loop represents higher level control that is more closely associated with voluntary control. This loop is associated with the greatest level of computation and flexibility and is subject to the longest delays. The goal of the system is to produce enough net torque to effectively balance the inverted pendulum. The total torque produced by all three loops in the system is sometimes referred to as the 'effective stiffness'.

To avoid confusion, we must firmly distinguish between passive stiffness and effective stiffness. Passive (or intrinsic) stiffness concerns only the innermost feedback loop in the system whereas effective stiffness concerns the combined effort of the whole system. The effective stiffness could conceivably be produced by any combination of the three loops or by any one of the loops in isolation. The effective stiffness is thought to be approximately

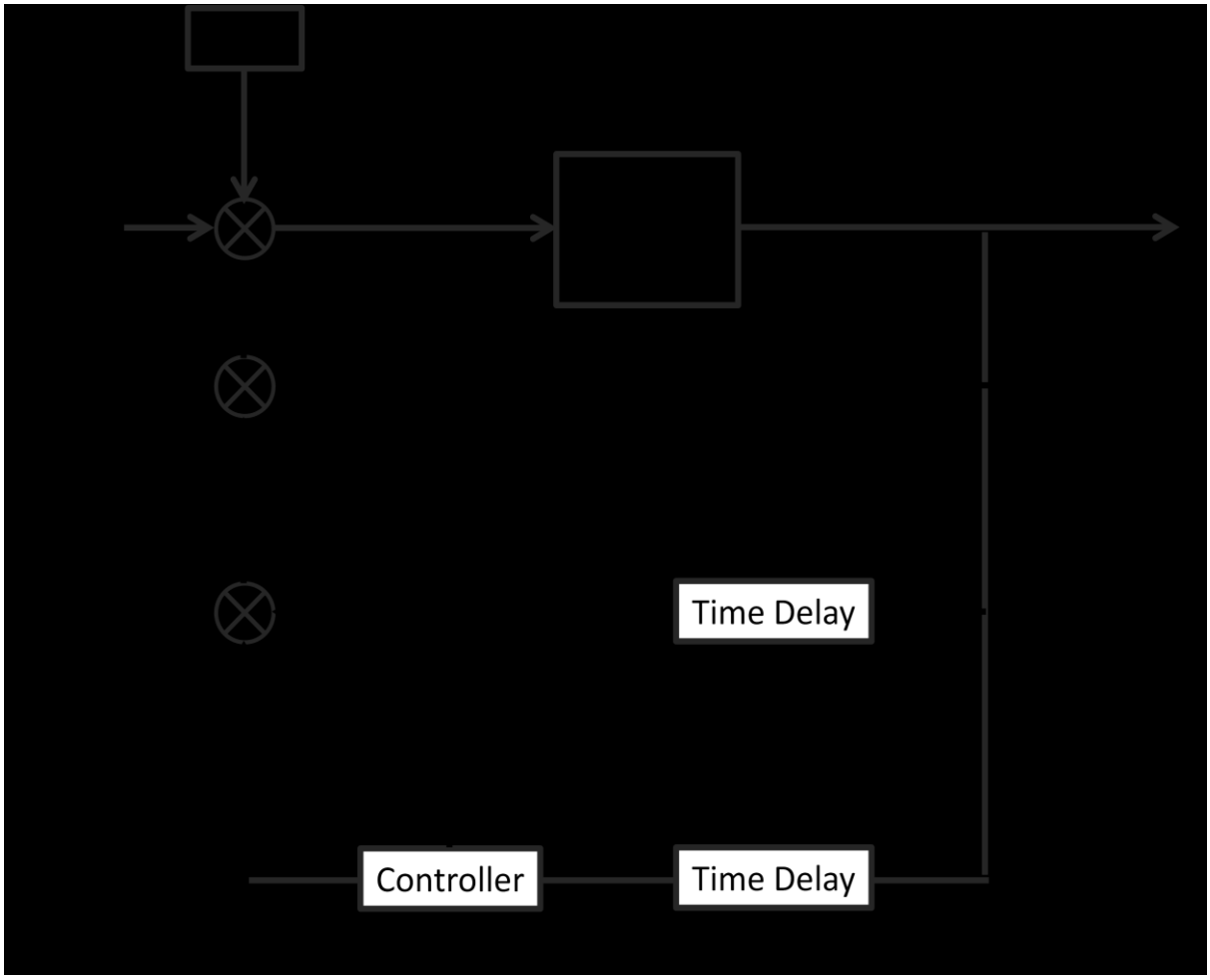

Figure 2. Parallel loops in human balance control.

This conceptual model groups the balancing mechanisms into three groups: 1) the passive restoring forces, 2) simple and complex reflexes, and 3) higher level control. All mechanisms are available for balance control but the contribution of particularly the reflex and higher level loops is still the subject of much debate.

200 % of *mgh* (Morasso & Schieppati, 1999; Loram & Lakie, 2002*b*). An effective stiffness of this magnitude explains the relatively small sway size, and quite characteristic sway frequency that is observed in quiet standing (an inverted pendulum passively stabilised by a spring with stiffness 200 % *mgh* will produce realistic sway size and frequency). If the torque provided by the passive loop is less than *200* % mgh then the system requires neural assistance from the reflex or voluntary loops to explain the sway characteristics. Thus, we can only discount the reflex and voluntary loops if we find that the passive stiffness of the system is very large (200 % mgh). However, if this was so then there would be the difficulty in accounting for the sway that is observed because a passively stabilised system will only sway if perturbed in some way. What is its cause? It seems most likely that the source of the sway is inherent to the neural component. It may be an unwanted random component ("noise") or it may reflect some purposive aspect of the way that the neural component is generated (Loram *et al.*, 2005*b*).

Passive control

To what extent does passive ankle stiffness contribute to the total effective stiffness in upright stance? Passive stiffness is an attractive control mechanism because it does not involve any neural transmission and consequently is not associated with any time delays. Winter *et al* (1998) proposed a simple a stiffness control model to explain quiet standing control. The authors suggested neural control was unlikely principally because 1) in their view perceptible sensory thresholds (Fitzpatrick & McCloskey, 1994) were too large to detect the small slow sways of quiet stance, and 2) the phase locked relationship between ankle moment and the motion of the CoM suggested the control system was not subject to time

delays. Further experiments appeared to support the view that ankle stiffness was the dominant restoring force in balance control (Winter *et al.*, 2001). However, such conclusions were subsequently shown to be questionable due to the inappropriate application of analytical methods to a closed loop system (Morasso & Schieppati, 1999; Morasso & Sanguineti, 2002; van der Kooij *et al.*, 2005). Additionally, the authors did not convincingly differentiate between passively and neurally generated torques.

Loram and Lakie (2002) provided the first direct estimate of ankle stiffness during quiet standing using appropriate methodology. When estimating passive ankle stiffness it is critical to use a method that excludes any neural contributions to torque modulation. The authors achieved this using a piezo-electric translator to apply small but rapid perturbations to the foot while subjects were freely standing. This method permitted clear separation of the instant passive torque response from any time-delayed neural responses, and enabled a true estimate of intrinsic ankle stiffness. This method revealed an estimated passive ankle stiffness of 91 ± 23 % (mean ± SD) of *mgh*. Due to the small size of the perturbations, this was considered relevant to the small high frequency components of sway observed in quiet standing (Loram & Lakie, 2002*a*), but not necessarily relevant to larger sways. Indeed, previous measurements of ankle stiffness in supine subjects have shown that stiffness markedly decreases as the size of ankle movements increase (Kearney & Hunter, 1982). This possibility was investigated by Casadio *et al* (2005) using considerably larger perturbations (1 degree amplitude, 150 ms duration). In this study the ankle stiffness was estimated to be 64 ± 8 % of *mgh which* suggests, in line with previous work (Kearney & Hunter, 1982), that ankle stiffness decreases as a function of ankle rotation amplitude during standing.

Despite these direct measurement approaches, several studies (Peterka, 2002, 2003; Maurer & Peterka, 2005; van der Kooij & van der Helm, 2005) estimated passive ankle stiffness to be considerably lower (10 – 15 % of load stiffness) than values reported above. These estimates were based on fitting transfer functions to ankle torque responses to continuous perturbations ranging from 0.5 to 8 degrees. However, it may be argued that sway sizes evoked by perturbations greater than 1 degree are not representative of the conditions of quiet standing, and that the stiffness values identified from such optimisation procedures are not relevant to quiet standing. Indeed, further work from Loram *et al* (2007) showed that very large ankle rotations (7 deg) do reveal a very low estimate of ankle stiffness (19 ± 5 %). Thus, we may conclude that during quiet standing, the innermost passive loop contributes quite significantly (between 50 and 90 % for sways between 1 and 0.055 deg) towards the total effective stiffness. The contribution by passive ankle stiffness may serve to assist the neural control mechanisms by reducing the time constant of the human inverted pendulum, but the remainder of the effective stiffness must be produced by active neural control.

Reflex control

Research into the neural control of balance largely relies on perturbation studies. Perturbing stance allows investigators to 'open the control loop' and study the response to the perturbation in the hope that the response reveals something about how balance is normally controlled (Van der Kooij *et al.*, 2005). Most experiments of this type have concluded that balance is controlled largely by reflexes (middle loop in Fig 2). The most direct evidence stems from animal work with the often explicit assumption that control mechanisms for this task are similar in different species (Deliagina *et al.*, 2007; Lockhart & Ting, 2007). It is known

that, after a period of training, spinal cats are able to maintain balance for a short period of ten seconds or so (Macpherson & Fung, 1999). This precarious form of stability relies primarily on the inherent stiffness of the tonically active extensor muscles, and simple spinal stretch reflexes. More robust balance similar to that observed in the intact cat, is found in the decerebrate cat (Bard & Macht, 1958). Thus it follows that (in the cat) the most simple reactive balance mechanisms are found in the spinal cord, and more complex components that allow greater flexibility of action are located in the brainstem and cerebellum. The brainstem and cerebellum permit integration of visual, vestibular and proprioceptive sensory inputs (Deliagina *et al.*, 2007) and allow more coordinated corrective responses, possibly due to the development of internal models (Macpherson & Fung, 1999). Deliagina et al (2007) suggest that lower level and higher level reflex loops work in parallel. In this configuration, lower level spinal reflexes driven by limb mechanoreceptors provide simple corrective motor responses, while higher level (brainstem and cerebellum) integrate proprioceptive, visual, and vestibular sensory information to provide more contextually sensitive corrective responses, with additional roles of controlling the gain of spinal mechanisms, and setting body configuration.

Similar methods have also been used to investigate human responses to perturbed stance. (Diener *et al.*, 1984) applied platform rotations around the axis of the ankle joints in healthy standing subjects. When the feet were rotated toes-up, they found short latency (55-65 ms) and medium latency (108 – 123 ms) neural responses in the triceps surae muscles. These responses were inappropriate and destabilising: both the perturbation and the resultant reflexes caused the body to topple backwards. However, a stabilising rescue response soon followed in the tibialis anterior muscle (130 – 145 ms). The authors suggested that all

responses were involuntary because the response times were reportedly faster than that of a voluntary reaction with similar triggers. The same pattern of results, albeit with slightly different delays has been found elsewhere (Nardone *et al.*, 1990). Other experiments with smaller perturbations failed to find short latency responses to ankle rotations but did show similar (120 ms) destabilising long latency responses followed by more functionally reliable responses after around 200 ms (Nashner, 1976). Tiny ankle rotations more relevant to the size, if not the velocity, of standing sway (0.055 deg) have been shown to evoke long latency (100 ms) destabilising responses but no short latency responses (Loram & Lakie, 2002*b*). The lack of short latency responses in the latter two experiments may reflect the smaller perturbation sizes used in these experiments. Evidence suggests that short latency reflexes mediated by Ia afferents do not contribute to stance control during quiet standing where sways are small and slow (Nardone *et al.*, 2000). Many subsequent studies have reported long latency corrective responses which are mediated by vestibular, proprioceptive and visual information in response to a wide variety of perturbations (Bloem *et al.*, 2000; Carpenter *et al.*, 2001; Cathers *et al.*, 2005). It is generally (Nashner, 1976; Diener *et al.*, 1984), though not always (Loram & Lakie, 2002*b*) reported that the gain of long latency responses can be modified to assist stabilisation. Thus, destabilising long latency responses can be attenuated, and similarly, facilitative responses can be enhanced to assist stability. Such modification does not occur immediately but through experience and appears to require healthy cerebellum function to be achieved (Nashner, 1976).

All these observations in human experiments may be interpreted in light of animal experiments (Deliagina *et al.*, 2007) where simple short latency spinally mediated reflexes occur in response to joint rotation and, depending on the perturbation type (platform

rotation vs. translation), can be destabilising. Longer latency and more functionally reliable responses may rely on more accurate estimates of 'task-level' variables such as the CoM state (Gollhofer *et al.*, 1989; Nardone *et al.*, 1990; Lockhart & Ting, 2007; Welch & Ting, 2008). Such estimations will necessarily be based on a wider range of sensory information and require higher level processing in the brain stem and cerebellum with potential input from the motor cortex (Taube *et al.*, 2006). Lower level destabilising reflexes can be attenuated by healthily functioning higher level centres (Nashner, 1976). Thus, the majority view suggests that balance control is achieved through predominantly long latency reflex loops with variable gain. Indeed, much research on human quiet standing has proceeded on these assumptions (Fitzpatrick & Taylor, 1992; Fitzpatrick *et al.*, 1992, 1994).

These ideas are also reflected in computational models of human balance control. It is commonplace to fit large swathes of experimental data with a pre conceptualised model of the balance control system. This technique can be used to estimate feedback gains and time delays of the human controller. The vast majority of authors model human balance control as a continuous feedback controller balancing an inverted pendulum (Peterka, 2000, 2002, 2003; Mergner *et al.*, 2003, 2005; Masani *et al.*, 2006; Maurer *et al.*, 2006; van der Kooij & de Vlugt, 2007). In this type of model corrective responses occur continuously in response to errors mimicking the continuous nature of the human reflex feedback loop. 'Proprioceptive' sensors detect and correct for velocity and position deviations with a time delay, and such simulations can produce realistic sway when injected with appropriate noise. More complex models include other sensory systems too (Peterka, 2002, 2003; Mergner *et al.*, 2005; Maurer *et al.*, 2006). These models can produce realistic balance reactions because 1) multi-sensory integration is used to respond appropriately to an array of perturbation types (e.g.

platform tilt vs. platform translation) and 2) different sensory thresholds mimic the temporal sequence of corrective responses often observed in human perturbation studies (Nashner, 1976; Diener *et al.*, 1984; Gollhofer *et al.*, 1989). One particular weakness of this approach is that different pre conceptions regarding control models will result in quite different estimates of model parameters (Gawthrop *et al.*, 2009). It is therefore crucial that direct physiological measurements are used to inform models rather than the other way around. Indeed, the aim of chapter 3 in this thesis is to provide direct experimental data on the thresholds of the nervous system that may be used to inform future balance control models.

Higher level control

Some authors have raised doubts about the relevance of perturbation studies to the control of quiet standing (Loram *et al.*, 2009*a*). The majority of experiments have used perturbation sizes, typically between 0.5 and 8 degrees, that are considerably in excess of the small sways present during quiet standing (Nashner, 1976; Diener *et al.*, 1984; Gollhofer *et al.*, 1989; Nardone *et al.*, 1990; Peterka, 2002; van der Kooij & de Vlugt, 2007; Welch & Ting, 2008). Large perturbations provide unambiguous information about joint angle and body position, and exceed the perceptible thresholds of all sensory modalities (Fitzpatrick & McCloskey, 1994). It is not clear that this is the case during quiet standing where sways are small (mean sway size 0.13 deg - Loram *et al.*, 2005*b*) and sensory information potentially ambiguous (Loram *et al.*, 2009*b*). Clearly large disturbances do stimulate peripheral reflex responses but it is unclear whether these findings should generalise to quiet standing. The lack of experiments using small perturbations may, in part, reflect the technical difficulties with measuring small responses. When examining the pathway of a specific reflex (e.g. Schieppati

& Nardone, 1997) it is preferable to use a perturbation that evokes a strong and unambiguous response. This allows the response to be clearly quantified in EMG signals which are noisy and variable (Clancy *et al.*, 2002; Farina *et al.*, 2004). To investigate quiet standing it is most ecologically valid to use a perturbation that does not significantly disturb the normal standing process. However, in doing so, small but physiologically relevant responses (for example very small but functionally useful reflex responses) may remain undetected and unreported. Thus methodological difficulties may be a barrier to conducting the most appropriate experiments.

Doubts regarding the validity of experimental methods that employ unnaturally large perturbations, in combination with new experimental observations, have led a group of authors to suggest that balance control in humans is dominated not by reflexes, but by higher level control (represented by the outer loop in Figure 2). These new ideas arose after the discovery that ankle stiffness was too low to passively stabilise the human body (Loram & Lakie, 2002*b*; Casadio *et al.*, 2005), and that the low stiffness was the result of a compliant tendon and foot (Loram & Lakie, 2002*b*; Loram *et al.*, 2007*b*). This new finding prompted an elegant experiment which aimed to investigate how balance control through a compliant linkage (e.g. a compliant tendon) is accomplished. Lakie *et al* (2003) asked subjects to manually balance a real inverted pendulum with low intrinsic stiffness. Balance was achieved by pulling on a handle which was attached to the inverted pendulum via a weak spring. This paradigm was designed to be analogous to standing: the hand represents the calf muscle pulling on a compliant spring (the achilles tendon) to balance an inverted pendulum (the human body). It was reasoned that this equivalent task might reveal some of the principles of quiet standing control. The experiments revealed two key findings: 1) low intrinsic

stiffness means that the movement of the load and the movement of the controller (the hand) are decoupled and on average they move in opposite directions, and 2) the load is balanced through apparently discrete hand movements at a rate of about two to three adjustments per second. The authors noticed key similarities between this manual control task and observations made over 60 years ago in manual tracking experiments.

(Craik, 1947, 1948) developed a thesis that humans operate as intermittent control servos. A key feature of intermittent control is refractoriness. The refractory period is the time for which the control output is not modulated by sensory feedback. A consequence of refractory periods is that control proceeds as a sequence of discrete ballistic control actions each of which has a minimum duration of one refractory period: control adjustments are made intermittently not continuously. This constrains the rate of corrective action and has been proposed to explain the limited frequency of control adjustments that are observed in human manual control. Vince and Craik demonstrated that humans behave this way in both pursuit and compensatory tracking tasks (Vince, 1948). When subjects were asked to maintain the position of a pointer that was subject to a continuous external disturbance, the frequency of corrective actions did not depend on the frequency of the disturbance signal, but instead remained relatively constant at 2-3 actions per second. Additionally, performance in the task (the mean tracking error) was found to be proportional to the frequency of the disturbance. That is, subjects were unable to correct for higher frequency disturbances due to their limited rate of corrective action. It might be argued that a low rate of corrective actions can be explained by thresholds if, for example, a visual disturbance is not detected until it has reached a certain amplitude. However, Craik (1947) found that

visual magnification of the disturbance signal during tracking tasks had no effect on the periodicity of corrective action.

This limited bandwidth of human voluntary control, where coherent responses are typically limited to a maximum of 2 Hz, has been convincingly demonstrated since (Neilson *et al.*, 1988; Loram *et al.*, 2009*a*, 2010), and is consistent with an intermittent control hypothesis (Gawthrop *et al.*, 2011). Direct evidence of refractoriness in human control has also been provided (Vince, 1948). Drawing on work by Telford (1931), Vince and Craik showed that, during a manual tracking task, when two stimuli are presented in quick succession, the response to the second stimulus is delayed when compared with the response to the first. This is explained if the system is refractory after responding to the first stimulus and must wait until the end of the refractory period before a response to the second stimulus can be formulated. The duration of refractoriness is commonly called the psychological refractory period (Pashler, 1994).

What is the cause of the psychological refractory period? Welford (1952) proposed that refractoriness may be explained through the inability to select two responses simultaneously. Stimulus and response may be considered in three temporally consecutive stages: 1) perception of a given stimulus, 2) the selection of an appropriate response, and 3) the execution of that response. Welford believed that it was impossible for two response selection phases to occur in parallel: they could only occur in series. The result is that if two stimuli were presented in quick succession, the response planning to the second stimulus did not start until the response planning to the first stimulus was completed. Many subsequent experiments have provided evidence in support of this theory and have shown the effect to

be robust regardless of sensory modality or of the nature of the response (Pashler, 1992, 1994).

The rate of corrective actions observed in manual balancing of a real inverted pendulum (Lakie *et al.*, 2003) suggests that in this task human control is subject to a refractory period and is engaging the same higher level intermittent control process as during manual pursuit tracking (Vince, 1948; Loram *et al.*, 2012). If manual balance control in humans is achieved by intermittent control, we would expect the rate of corrective actions to remain constant regardless of the nature of the feedback, or of the dynamics of the load. These questions were addressed by further experiments. Lakie and Loram (2006) demonstrated that the rate of control actions did not change when subjects used visual, vestibular or proprioceptive sensation either alone or in combination. Loram *et al* (2006*a*) showed that the rate of corrective actions did not change substantially when the time constant of the inverted pendulum was changed by a factor of two. Thus it may be concluded that manual balance of an inverted pendulum involves a common neural process that is consistent with the intermittent control servo hypothesis first postulated by Craik (1947). The question now turns to real standing: are the characteristics of quiet standing control are also consistent with a higher level intermittent control paradigm?

Answering this question became possible with the development of novel techniques to track dynamic ultrasound images of the calf muscles (Loram *et al.*, 2006*b*). This enabled a direct measurement of calf muscle fluctuations during unperturbed standing. First it was demonstrated that, on average, the body and the calf muscle move in opposite directions (consistent with manual balance of an inverted pendulum through a compliant linkage).

With exaggerated sways, when the body leans forwards the calf muscles contract, and when the body leans backward the calf muscles lengthen – a phenomenon the authors described as 'paradoxical muscle movements' (Loram *et al.*, 2004). This was also shown to be the norm during the small sways of quiet standing (Loram *et al.*, 2005*a*). Additionally, and most crucially, the same study revealed the calf muscle makes adjustments at a mean rate of about two to three per second. Thus, the control of quiet standing is inconsistent with at least the simple stretch reflex control paradigm because of paradoxical muscle movements, and control is consistent with the same intermittent process that is observed during manual tracking and balancing tasks (Loram *et al.*, 2009*c*).

The true mechanisms of human standing control are still not known and there is substantial resistance to the intermittent control hypothesis (Maurer & Peterka, 2005; Maurer *et al.*, 2006; van der Kooij & de Vlugt, 2007; Mergner, 2010). Current evidence for intermittent control in standing remains circumstantial. However, there are a number of reasons why intermittent control may be preferable to a continuous reflex-like control paradigm. For example, continuous negative feedback servos have an increasingly narrow stability margin as time delays grow larger (Bottaro *et al.*, 2008) whereas intermittent control is considerably more robust (Gawthrop *et al.*, 2011). This is relevant in biological systems because feedback time delays can be substantial (Loram *et al.*, 2009*a*). Additionally, the discrete sequence of pulsatile control actions that are associated with intermittent control may allow for higher quality feedback than continuous control. Evidence for this comes from a manual control task.

Loram *et al* (2010) asked subjects to manually balance an inverted pendulum with a joystick using one of two methods: 1) Subjects maintained continuous contact with the joystick or, 2) subjects gently tapped the joystick. While the authors believe that human manual balancing is intermittent regardless of the control method, the tapping method is unambiguously intermittent control. This method also exaggerates the pulsatile nature of human control by forcing subjects to control with discrete ballistic actions. The gentle taps method was shown to be slightly superior to the continuous contact method, and was significantly more robust at compensating for unexpected changes in controller gain. This may be explained if control by gentle taps allows periods of higher quality feedback. When tapping the joystick, the subject is not in continuous contact with the joystick. This means there are periods of time where their own motor noise is removed and they can distinguish between their own actions and the movement of the load. This alternation between action and sensation allows the subject a clearer understanding of the cause and effect of their own motor actions, and a greater ability to understand the properties of any external disturbances that are acting on the load. This is important because biological motor control is subject to considerable 'external disturbances' such as nonlinearities caused by short range muscle stiffness (Hill, 1968; Campbell & Lakie, 1998; Lakie *et al.*, 2012) and other dynamic motor properties (Maganaris *et al.*, 2000). Alternation between sensation and action may also be biologically relevant. For example, it has been shown that sensory perception is attenuated during active movement (Chapman *et al.*, 1987; Collins *et al.*, 1998). This may be related to pre-synaptic inhibition of sensory afferents to the spinal cord (Seki *et al.*, 2003) and even to the expectation of voluntary movement (Voss *et al.*, 2008). An intermittent control strategy is therefore well placed to cope with the many and varying demands of controlling a biological

system and may offer a more appropriate explanation for human feedback control than a more conventional continuous control paradigm.

Concluding remarks

In this introduction we have discussed potential mechanisms of human balance in the context of a simplified conception of the human balance controller (Fig 2). We have suggested that the contribution of the innermost loop (passive loop) is now known but that the relative contribution of both the middle reflex loop and outer higher level loops is not yet known. In the subsequent experimental chapters of this thesis, we investigate the roles of reflexes and higher level control in human balancing.

In the first experimental chapter we tackle a difficult methodological technique that is particularly useful in balance control investigations: automatic analysis of dynamic ultrasound images. We apply novel commercial tracking software to the task (Osborne & Lakie, 2011) and find it to be accurate, precise, and crucially more time efficient than previous methods (Loram *et al.*, 2006*b*). In the second experimental chapter we investigate the sensitivity of the neural control loops in human standing. We apply a small perturbation to standing subjects and, using our newly developed tracking technique, identify the very earliest neural response to the perturbation. In the third experimental chapter we investigate the relative contributions of reflex and higher level control to human balance control and we use simple modelling to provide a plausible explanation for our experimental findings. Finally, in the fourth experimental chapter we move to a more abstract level and investigate the properties of higher level manual balance control. In particular, we

investigate the dynamic nature of sensory feedback and discuss the possible implications to standing balance control.

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Chapter 2

A NOVEL PLANAR TRACKING TECHNOLOGY FOR PHYSIOLOGICAL IMAGE ANALYSIS

ABSTRACT

Automated image tracking provides new insights in many physiological studies, but present methods are ad hoc and can be difficult to use. They are generally based on following the movement of one or more specific regions of interested - point tracking. We tested newly available novel planar tracking technology commercially developed for the special effects industry, which does not use point tracking. We validated the tracker and made two dynamic physiological measurements. Our validation measurements describe the accuracy and repeatability of the technique, and our physiological measurements demonstrate the flexibility of the software. Our results suggest that planar tracking may be of particular use with techniques that produce low quality images such as ultrasonography.

Introduction

Automated image tracking techniques have proved increasingly valuable in numerous areas of physiological research and clinical diagnosis. For example, automated tracking of ultrasound images has enabled dynamic measurements of skeletal muscle length which reflect alterations in neural drive (Loram *et al.*, 2006) and has also been used to follow changes in vascular diameter which reflect neural control (Beux *et al.*, 2001). Tracking techniques are used widely in cellular biology for measuring movement of proteins, vesicles and cells (Miura, 2005).

Despite these successes, existing tracking techniques are restrictive. Tracking tools designed for scientific investigation are often limited to making one specific type of measurement. A tracker that performs well at one task will usually require substantial modification by a skilled programmer in order to perform satisfactorily in a different task. In addition, current techniques, most of which rely on 'point tracking', frequently suffer when 1), selected points of the object being tracked move out of frame, or lose definition, and 2), parts of the image being tracked distort or change shape. This is a particular problem for tracking 3 dimensional objects with a 2 dimensional scanner. Accurate 2-D registration of tracked points cannot give an accurate picture of how the object moves when it moves out of the plane of measurement. Unfortunately, loss of tracked points, poor definition of points and movement out of the plane of the recording are common features of biological imaging. A new tracking technology that is more flexible in scope, and more robust in dealing with distortions and low quality images, may facilitate the analysis of moving biological images and permit analysis of images that were previously judged untrackable.

Our group has previously published a method for automatically tracking dynamic ultrasound images of Soleus and Gastrocnemius muscle (Loram *et al.*, 2006). This method has proved successful but has a number of limitations. Firstly, the user needs a grasp of MATLAB programming. Secondly, it is limited in scope: the programme would require significant modification to track objects other than these muscles. Finally, and most significantly, it is based on multiple point tracking which has the disadvantages above and is computationally intensive and slow.

Here, we apply a recently developed novel commercial tracking technology designed for the special effects film industry to scientific investigation. We aim to test the utility of the technique using a biologically appropriate model, and to show that the technique, which demands no specialised computer knowledge or equipment, is flexible and may be suitable for use with techniques such as ultrasonography which generate low quality images.

Methods

Software description

The tracking software used in this paper, *Mocha for After Effects V 2.6- Single User Version* (Imagineer Systems - http://www.imagineersystems.com/products/mochaAE), is an offline tracking tool that employs a unique technology known as planar tracking. Existing tracking software generally requires the user to identify 'points' on an object that are suitable for tracking. Instead, Mocha tracks an object's movement based on a user defined plane: a virtual two dimensional surface where movement is described by translation, scale, rotation, shear and perspective of a virtual object. Thus, tracking of objects is based around their

modelled movement in the plane in which movement occurs, and not by the movement of specific points.

Once a plane is defined, the automatic tracking process takes place: first, correlation establishes the gross translation, rotation and scale to a pixel level accuracy; the correlation result is then optimised via an iterative process which uses a least-squares method to find the optimum projective warp to align the source and destination images. During this process, in addition to tracking from one frame to the next, the tracker goes back five frames and tracks the t-5 frame into the current frame to help minimise drift. Once the automatic track is complete, an adjust track tool allows the user to instantly check and semi-automatically compensate for drift. With this technique, accurate tracking is possible even when specific features of an object may become distorted or obscured; a feat not easily possible with previous tracking tools.

Stretched spring experiments

In order to test the efficacy of the tracker we wanted to create situations relevant to real physiological measurements. The key features are that biological images typically lack well defined, unchanging and constantly in focus points that can be used as single or multiple targets. The Mocha tracker is not a point tracker and should deal with movies where the image is poorly defined and subject to change. This is typically the case when tracking moving muscles (Loram *et al.*, 2004, 2005, 2006) so we used a phantom which mimics this.

A small extension spring was held in a water filled polyethylene beaker between two taut lengths of wire (Fig. 1). One end of the spring was attached to the bottom of the beaker and

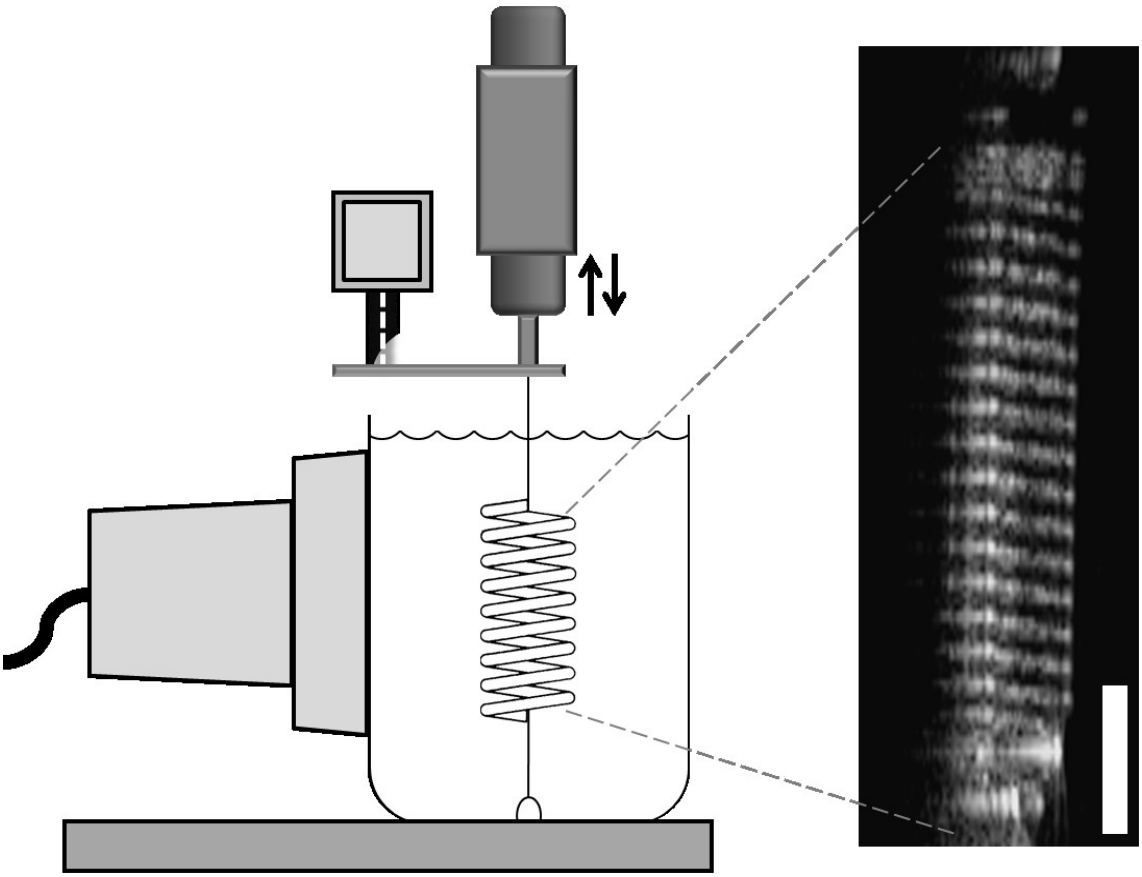

Figure 1. Experimental setup.

An ultrasound probe (USP) views a spring being moved by a servo motor (SM). A Laser rangefinder (L) measures movement of the spring. In the ultrasound image the white bar represents 1cm.

the other end was attached to a servo motor. The attachment extended horizontally outward so that a laser range finder (YP05MGVL80, Wenglor Sensoric, Germany, resolution < 2 µm), mounted vertically above could measure the displacement of the spring. An ultrasound probe (5-10 MHz probe, DIASUS) was mounted in a vertical plane, attached to the beaker, such that stretches of the spring occurred in the plane of the probe, producing the phantom image. The ultrasound machine produced videos that were saved as AVI files at a frame rate of 15 frames/s with pixel dimensions of 138 x 138 µm. To allow comparison with tracking outputs from the ultrasound technique which were sampled at 15 Hz, data obtained with the laser range finder was low pass filtered (4^{th} order zero-phase Butterworth, 6Hz cut off) before being down sampled to 15 Hz.

We first aimed to test the accuracy and repeatability of the tracker/ultrasound combination. To this end we devised two different tests: a static test where the spring was stretched to specific lengths and held in position; and a dynamic test where the spring was stretched using filtered white noise. We describe the procedures below.

Static spring test

In the static test, the spring was stretched in equal steps and held in position between each stretch (see Fig. 2A and B). During each trial, the spring was stretched three times resulting in a 'three step staircase', with each stretch lasting 2.5 seconds, and each hold lasting 4 seconds. Within each trial step sized remained constant, but between trials step size was varied between 10, 25, 50, 100, and 250 µm. Each of the five resulting videos was tracked five times by the same operator.

Dynamic spring test

In the dynamic test, the spring was stretched by a randomly generated waveform. The advantage of a dynamic test is that we are able to test how the repeatability of the technique may vary at different frequencies. The test also approximates most closely to the way in which the tracker is likely to be applied in a neurophysiological context, because it tracks movements occurring at continuously changing velocities. The input to the servo was filtered white noise (low pass 4^{th} order Butterworth filter with 4 Hz cut-off) for a 30 second duration. The rms amplitude of spring movement was 624 μm. The resultant video was then tracked five times by the same operator. All software settings were identical in all stretched spring experiments.

Physiological experiments

We performed two physiological experiments where measurements were made using the tracker. The experiments were: measuring small changes in tibialis anterior muscle length (< 4 mm) using an ultrasound probe; and measuring brachial arterial diameter using ultrasound when resting (diameter changes < 3.5mm) and during exercise (diameter changes plus vessel movement < 11mm). All subjects gave written informed consent, and the study was approved by the local human ethics committee and conformed to the principles of the Declaration of Helsinki.

Muscle length

In this experiment we aimed to test how well the software tracked human skeletal muscle length changes. We used actively generated torque as our reference value with the

expectation that small length changes of the muscle would, to a reasonable approximation, linearly reflect torque under isometric conditions (Loram *et al.*, 2007). A subject rested supine on a couch with both legs extended. The sole of the right foot was held against a vertical metal plate with Velcro ® straps so that a stiff strain gauge transducer recorded ankle torque produced by attempted dorsiflexion. To minimise deformation of the foot during the trial, the subject's right foot was first splinted by taping a rigid sheet of plastic to the sole of the foot. A computer monitor provided real time feedback of the subject's torque level via a digital oscilloscope using Simulink software. An ultrasound probe (as above) was placed on the belly of tibialis anterior muscle of the right leg aligned with the shin and perpendicular to it. In this position, the probe provided a longitudinal view of the pennate structure of the tibialis anterior muscle.

The subject was asked to track two patterns of torque modulation in separate trials: 1) a slow linear ramp from a baseline level (normalised to 0 Nm) up to 10 Nm over 20 seconds; and 2) a sawtooth-like waveform with three discrete shorter ramps from 0 to 10 Nm over a period of 30 seconds. We chose these tasks to mimic postural (slow ramp) and dynamic (sawtooth) conditions of muscle control. The subject was able to familiarise himself with the setup until he was comfortable that he could reasonably control his torque output whilst avoiding co-contraction. He then performed each task three times. Under these isometric conditions muscle length changes were small (< 1.5 mm). In each condition, the trial where actual torque was closest to target torque was chosen for analysis. Each video of muscle length was tracked five times by the same operator.

Arterial diameter

For the purpose of comparison the ultrasound system was used in combination with an established real time arterial diameter measurement technique (Beux *et al.*, 2001) to provide a continuous measurement of the brachial artery diameter. A subject lay comfortably supine with his left arm abducted 45°. The brachial artery of the left arm was scanned longitudinally using a Doppler ultrasound probe (8 Mhz probe, Phillips Envisor USA) placed approximately 3 cm proximal to the elbow joint. In addition, a second ultrasound probe (5-10 MHz probe, DIASUS) was placed approximately 2 cm proximal and perpendicular to the first to provide a cross sectional view of the brachial artery. Ultrasound video was obtained 1) during 15 seconds of rest, and, 2) for 15 seconds whilst performing a light rhythmic hand grip exercise. The handgrip exercise condition created a challenging test for the tracking software because of the large movements of the artery caused by muscle contraction.

Data analysis

Analysis using Mocha software was carried out offline and the output of the programme (4 coordinates per frame defining the tracked virtual object) was reconciled with data recorded from other sensors using MATLAB software. Data obtained using the Mocha tracking software was low pass filtered (4^{th} order zero-phase Butterworth, 6 Hz cut off) prior to subsequent analysis. The software settings allowed the tracker to search for translations, changes in scale, rotations and shear, and were kept constant throughout all our experiments. Typically, automatic tracking proceeded at 5 to 6 frames/s and was followed by quick (< 5 minutes per track) semi-automatic adjustments. For the stretched spring

experiments, we purposely limited our post tracking adjustments to < 2 minutes per track to keep the procedure quick and consistent. We also performed cross spectral analysis using techniques developed by Halliday *et al*, (1995) with Neurospec 2 software (http://www.neurospec.org). This analysis technique reveals the relationship between the input signal (laser range finder) and the output signal (Mocha analysis) at different frequencies. Specifically, the gain describes the relative accuracy of the measurement at different frequencies. A perfect accuracy would result in a gain of 1 at all frequencies. All results are presented as the mean ± standard deviation unless otherwise stated.

Results

Stretched spring experiments

Static spring test

In the static test we stretched the spring in three step 'staircases'. We used five different step sizes (10, 25, 50, 100, and 250 µm) resulting in five different 'staircases'. Each of the five resulting 'staircase' videos was tracked five times by the same operator. Figures 2A and 2B show two examples of these tests. Figure 2A shows the 250 µm step size, and figure 2B shows the 10 µm step size. These plots have been filtered for clarity. The figures show the mean (grey solid line) and standard deviation (grey dashed lines) of the five tracks of each video. Actual spring length as measured by the laser rangefinder signal is also plotted (black dashed line). With the larger steps (250 µm – Fig 2A) the steps are obvious in the tracker record, and resemblance of the laser signal and the tracked signal is clear. For very small steps (Fig. 2B - 10 µm), the three steps as measured by the laser rangefinder (dashed black

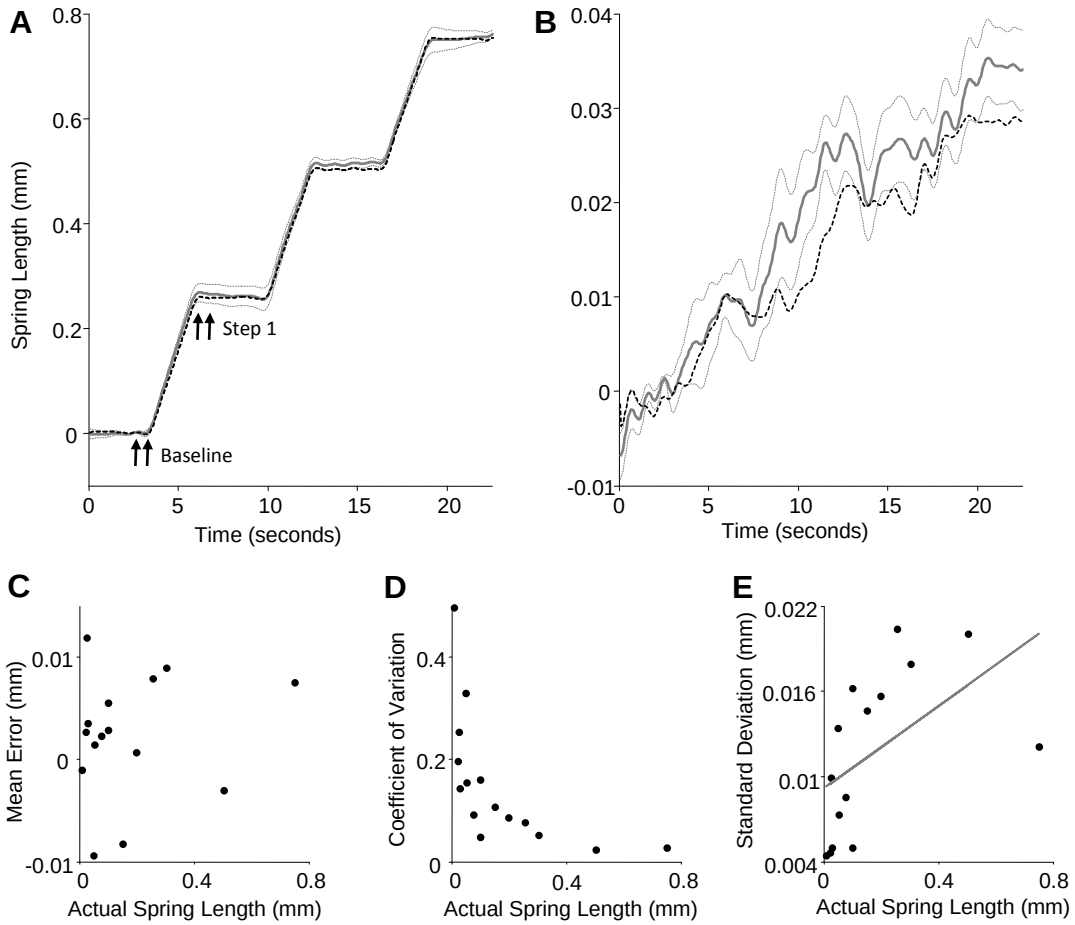

Figure 2. Static spring test.

A, shows spring length as recorded by the laser range finder (dashed black line), and the mean (thick grey line) ± SD (dashed grey lines) for 5 tracks of spring length estimated by the tracker for three 250 µm steps. B, shows the same for 10 µm steps. C shows the mean error of each tracked spring length plotted against actual spring length. D shows the coefficient of variation plotted against actual spring length. E shows the standard deviation at each measured length (relating to plot C).

line) are much less clear. This represents a limitation of the positional accuracy of our servo system which does not follow very small command signals particularly well. Nevertheless, the mean value obtained by tracking analysis (full grey line) mirrors the mean actual movement reasonably well and the three steps can be discerned. We wished to compare actual spring length with tracked spring length at each step. To calculate spring length at each step, we averaged the first ten points after each step (for example - Fig 2A - the values between the two arrows labelled 'Step 1'), and subtracted a baseline value (Fig 2A – first ten points before the first step - between two arrows labelled 'Baseline'). We did this for each of the three steps in each of the five different 'staircases'. This resulted in a total of 15 (3 x 5) different spring lengths with which we could compare tracked length with actual length. The tracking error was then quantified at each length as the difference between actual spring length and tracked spring length.

Mean tracking errors are plotted against spring length in Figure 2C. Where the errors are greater than zero the tracker has overestimated spring length, and when the errors are less than zero the tracker has underestimated spring length. The total mean tracking error was 2.2 ± 14.2 µm meaning that on average the tracker slightly overestimated spring length. However, this error was not significantly greater than zero ($p = 0.088$, one tailed one sample t-test) meaning we cannot be sure it is a genuine systematic error. Mean error did not significantly correlate with spring length irrespective of sign ($p = 0.54$). The mean error magnitude, calculated by averaging the absolute values of tracking errors, was 11.0 ± 9.1 µm. This gives an indication of the likely size of errors but no information on the direction. We quantified the linearity of the relationship between actual spring length and mean tracked spring length using the product moment correlation coefficient. We found a very

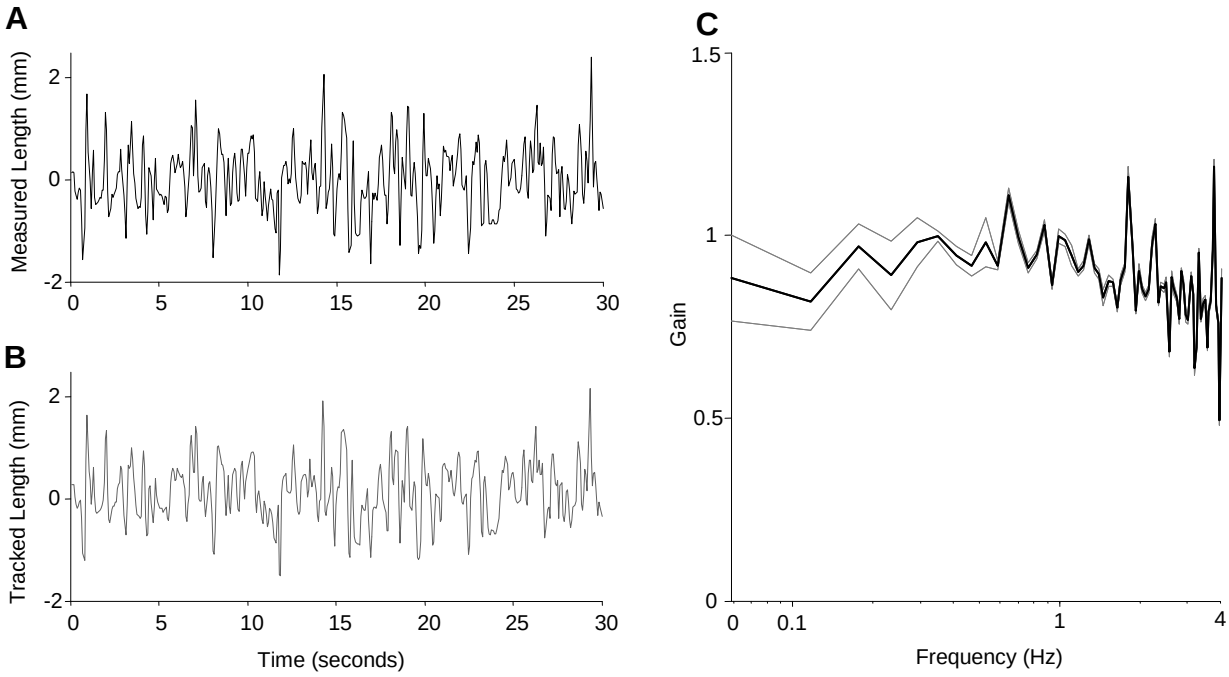

Figure 3. Dynamic spring test.

A, shows a trial of spring length (mm) as measured by the laser rangefinder and B shows the spring length (mm) as measured using the tracker. C, shows the gain between the tracked values and the measured values. The mean (black line) and standard deviation (grey lines) are plotted for five tracks of the same video.

strong relationship (r = 0.9996). Figure 2D shows the coefficient of variation plotted against spring length. The coefficient of variation is initially high but rapidly drops as the size of the movements being measured increases. Figure 2E shows the standard deviation plotted against spring length: did the tracking process become less repeatable as a function of spring length? Here, we found a moderate significant correlation (r = 0.53, p = 0.043, slope = 0.0144).

Dynamic spring test

Figure 3 illustrates a typical result from the dynamic spring test showing spring length as measured by the laser range finder (Fig. 3A), and as calculated by the ultrasound probe/tracking software combination (Fig. 3B). The mean scanner delay time of 126 ms, as obtained by cross correlation, has been subtracted. The aim of this test was to examine tracker performance over a range of frequencies. Consequently, we calculated the gain between the input signal (laser) and the length changes calculated by the tracker. Figure 3C shows the mean gain (black line) ± the standard deviation (grey lines) between measured spring length and tracked spring length for 5 tracks of the same video. Gain is closest to 1 between approximately 0.3 and 1.5Hz, and the variance is clearly largest at low frequencies. Above 1.5 Hz mean gain slowly declines and the error increases.

Physiological Experiments

Muscle Length Experiment

Figures 4A-C show the results of the force tracking task for the slow ramp waveform. The target and subject-generated torque is shown in Fig 4A and the corresponding tracker output

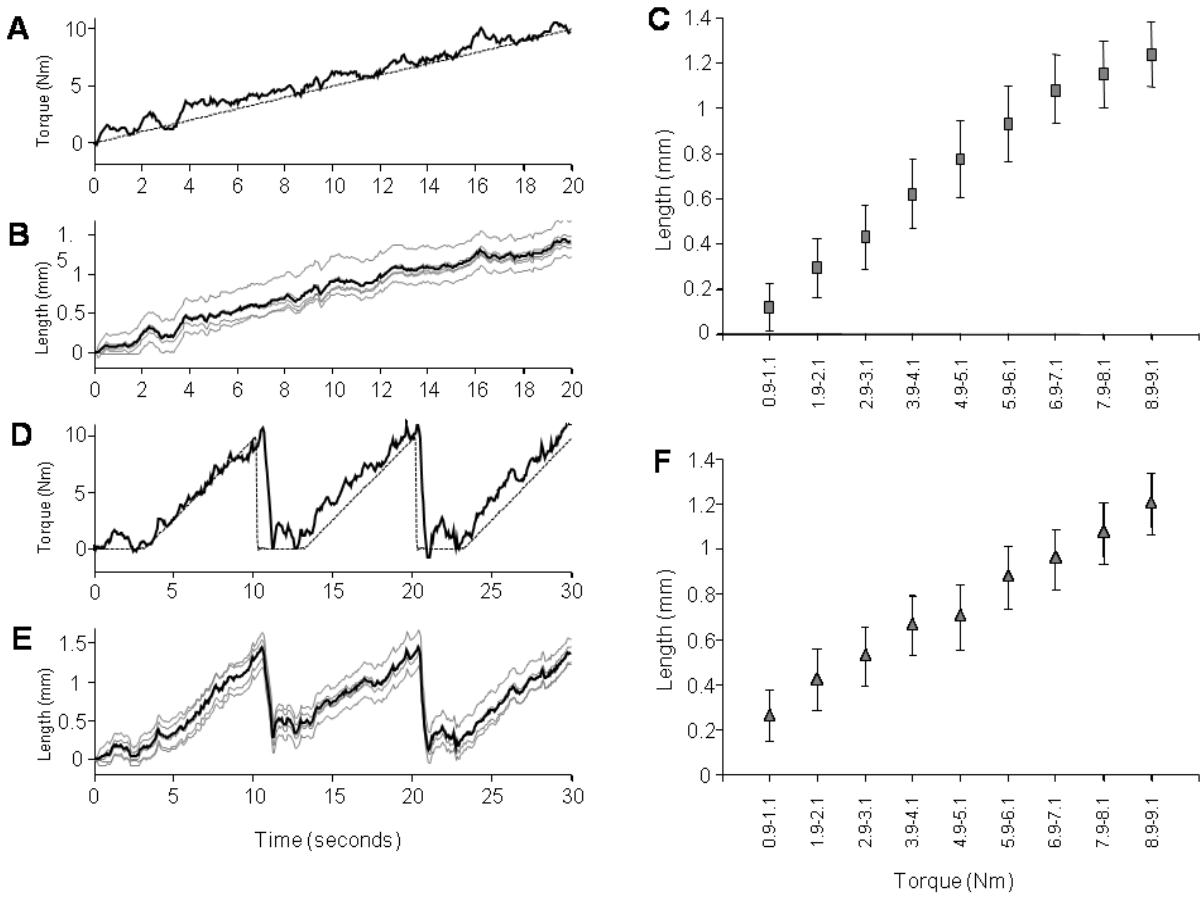

Figure 4. Muscle length test.

A, shows the desired torque level (dashed black line), and the recorded torque level (grey line). B, shows change in muscle length estimated by the tracking software. Each grey line is a separate track and the black line shows the mean of five tracks. C, shows tracked muscle length plotted against torque. Values of tracked length have been collected in bins. The bins vary by torque value and are shown on the x axis. D, E and F show the same for the saw tooth task.

of five separate tracks of tibialis anterior muscle length in 4B. The mean of the five tracks is plotted as a black line and each individual track is plotted as a grey line. Figure 4C shows the results of five tracks of muscle length plotted against torque. The data in this plot has been binned (as shown by the labels on the x axis) for clarity. The figure shows a strong linear relationship between muscle length and torque, although at higher torques there is less muscle length change per unit torque change than at lower torques. The relationship between muscle length and torque was described by a mean r^2 value of 0.98 ± 0.013, and a mean slope of 0.143 ± 0.012. Figures 4D-E show the same results for the sawtooth waveform. Here, the relationship between muscle length and torque was described by a mean r^2 value of 0.93 ± 0.007, and a mean slope of 0.116 ± 0.006. A two sample t-test revealed that there was a significant difference in slope between the sawtooth and slow ramp waveform conditions ($p = 0.004$).

Artery Diameter Experiment

Figure 5 shows the results of the arterial diameter experiment. In this experiment we had no absolute reference value against which we could check tracker performance. Instead, we tracked arterial diameter using an existing, clinically validated technique (Beux *et al.*, 2001) and used these results as a point of comparison. The technique by Beux *et al* (2001) uses an automatic algorithm to find and track the edge of the artery walls, and calculate arterial diamter in real time. As an additional measure of tracker quality, we wanted to quantify the within trial variability. When tracking arterial diameter for a short period at rest, we would expect fluctuations in diameter to be repeatable between cardiac cycles. Consequently, we

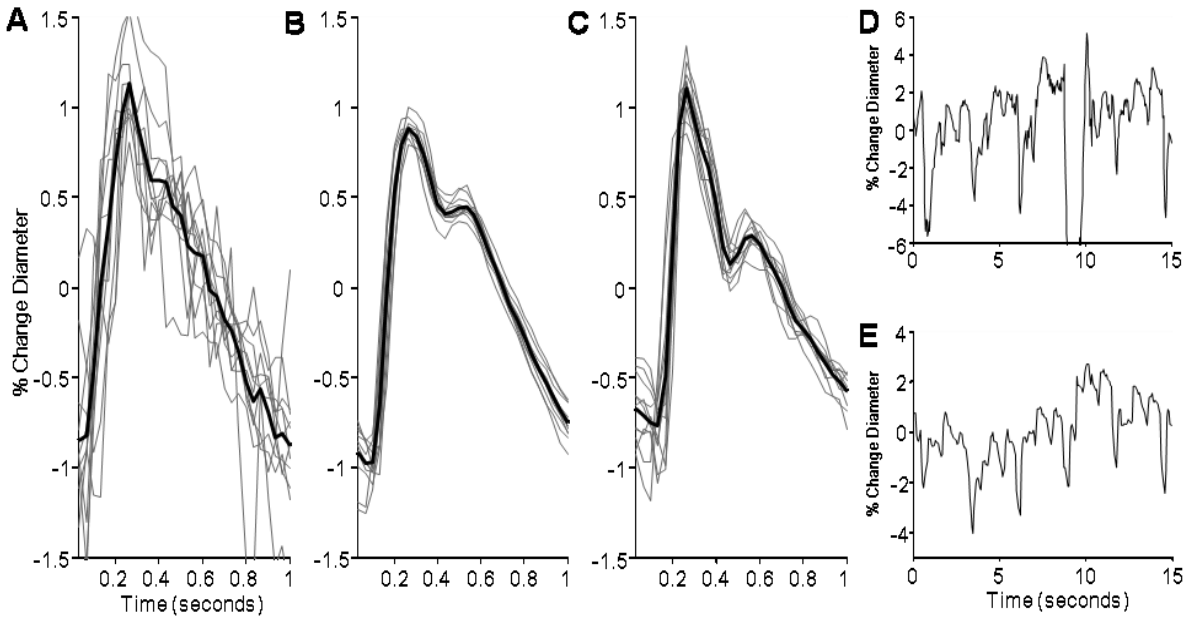

Figure 5. Arterial diameter.

A, shows the mean (thick black line) percent change in arterial diameter over 11 cardiac cycles measured with the technique described by Beux et al at rest. The thin grey lines show each individual cardiac cycle. B, shows the same tracked by Mocha. C, shows the same trial again but using a cross sectional view, tracked with Mocha. D and E show percent change in diameter during exercise; D is tracked using the technique by Beux et al; E is tracked using Mocha via a cross sectional view.

split each track up in to its constituent cardiac cycles (n = 11) and compared within trial variability between tracking methods.

Figure 5A shows the results obtained using an established automatic real time arterial diameter technique (Beux *et al.*, 2001). The thick black line is the mean of all cardiac cycles and the thin grey lines show each individual cycle. The mean diameter change throughout the cardiac cycle (largest value at point of dilation minus smallest value at point of constriction) was 2.32 ± 0.48%. The mean standard deviation throughout the cardiac cycle was 0.31 %. Figure 5B shows arterial diameter measured using Mocha software on the same ultrasound video. Here, the mean change in arterial diameter was 1.83 ± 0.18 %, and the mean standard deviation throughout the cardiac cycle was 0.09 %. Figure 5C shows the same trial but using a cross sectional view of the brachial artery obtained using the Diasus ultrasound probe and Mocha tracking software. Here, the mean change in arterial diameter was 2.00 ± 0.20 % and mean standard deviation over the cardiac cycle was 0.13 %. Figures 5D and 5E show change in arterial diameter during light rhythmic handgrip exercise measured with two techniques simultaneously: longitudinally by the real time technique; and via a cross sectional view using the Diasus ultrasound probe and Mocha software. The technique using Mocha maintains a track throughout the trial and the effect of the six handgrips can be clearly seen whereas the signal is lost between 7.5 and 10.5 seconds using the real time technique.

Discussion

We have validated a new, commercially available, and simple to use motion tracking technique. This unique technology, planar tracking, shows potential as a new method for studying biological phenomena where image quality is poor and traditional point trackers

are unusable. It is typically difficult to track movement and changes in biological objects. A key strength of this new technology is its ability to deal well with stretches, distortions and rotations in addition to translations. The spring phantom demonstrates this well because the stretching of a spring is a distortion of an object rather than a simple translation. The technique has been used here to measure movements of a few millimetres or less, occurring rather slowly. Accordingly the values that we calculate for accuracy etc are specific to the images that we tracked; other scanners or image capture devices can be used to provide any desired degree of accuracy.

Our results with the spring phantom provide the basis for a discussion of the utility of the tracker. We begin with the accuracy and repeatability of the technique based on the static test. Accuracy is described by how close, on average, the tracked values of spring length are to the true values of spring length: a mean error of zero would mean perfect accuracy. We found the mean tracking error of this technique to be 2.2 µm. This error was not statistically different from zero suggesting that, with our setup, the tracker does not systematically over or underestimate spring length but produces a distribution of errors that are random in direction (see Fig 2C). There was also no trend for the mean error to change as a function of spring length meaning the accuracy of the technique remained constant over the range of lengths we measured. Repeatability is described by the spread of the error distribution. We found a standard deviation of 14.2 µm suggesting that ~ 95% of all measurements will fall between -26.2 and 30.6 µm of the true measurement value. This is confirmed by the fact that 71 of the 75 measured values (94.7 %) were within this range. These values are most meaningful when expressed relative to the size of movements being measured. This is captured by the coefficient of variation (Fig 2D) which declines sharply to below 10 %

between 100 and 200 μm. We also found a significant correlation between the standard deviation of repeated measures and spring length (Fig 2E). This suggests that as the spring is lengthened the technique becomes slightly less repeatable. This may reflect the fact that stretching a spring is a distortion of an object rather than a simple translation. As the stretch size increases the spring distorts further from its original shape resulting in a greater challenge to the tracker, and larger errors.

We also wanted to examine the dynamic performance of the tracker. To do this, we stretched the spring with a filtered white noise input limited to 4 Hz, and used cross spectral analysis to calculate the gain of the tracker at different frequencies. Figure 3C shows the gain between spring length as measured by the laser, and spring length estimated by the tracker. The mean (black line) and standard deviations (grey lines) of five tracks of the same trial have been plotted. The mean gain is generally close to 1 up to approximately 1.5 Hz, and then slowly declines thereafter. This is caused by the limited sampling rate of our ultrasound machine, and would be improved on with a faster image capture device. At higher frequencies the gain errors are larger. This is because our servo system heavily attenuated input frequencies much above 1.5 Hz meaning movements of the spring above this frequency were very small. This is consistent with the larger coefficient of variation we found in the static test when measuring very small length changes because it shows that the that the size of the errors remains relatively constant irrespective of the size of the movement being tracked (see Fig 2D). We also note that in this test mean gain is slightly below unity at low frequencies: on average the tracker underestimated these movements. However, we believe this is an idiosyncratic result because a tendency to systematically underestimate slow movements would have impacted on our static test measurements

which were also quite low frequency. If this were so, it would be reflected in Fig 2 C by a mean error less than zero which is not what we found. Thus we do not believe that tracker systematically over or under estimates slow movements.

Another feature of the low frequency gain is that it is more variable. This shows that the tracker is less repeatable at these low frequencies, and suggests that a proportion of the errors reported in our static test are likely to have arisen as a consequence of slow drift. Thus the error values reported in the static test are likely to overestimate errors associated with higher frequency movements. We also note here that it is possible to minimise drift by restricting the software to tracking translations of objects only (as opposed to translations, changes in scale, rotations, and shear). This restriction makes the software more akin to a traditional tracker (though still rather different in that the software is still not tracking points). If the aim was simply to track the movement of an object, this particular setting would be appropriate. The fact that the software does not require particular features or points to lock on to makes this an appealing choice for such simple tracks. However, we are most interested in the ability of the software to track objects which distort so we did not explore this restricted setting further.

What are the implications of the findings of our spring validation experiments? We suggest the tracker is not well suited to measuring very small and very slow components of movements on a trial by trial basis. However, as the errors are random in direction and not systematically different from zero, this limitation may be largely overcome by averaging multiple tracks. Our static test which is susceptible to errors induced by low frequency drift suggests that approximately 95 % of errors will fall between -26.2 and 30.6 µm of the true measurement value, with a mean error magnitude of 11.0 ± 9.1 µm. Our dynamic test

results suggest the tracker is more repeatable at higher frequencies, and that very small faster movements should be discernible on a trial by trial basis. Our static test also suggests that the repeatability of the technique is likely to slightly decrease as stretch size increases, though accuracy should remain unaffected.

The measurements of muscle length showed a strong linear relationship with torque in two different tasks (r^2 = 0.98 ± 0.013 for the slow ramp task and r^2 = 0.93 ± 0.007 for the sawtooth task). We note that in the slow ramp condition the muscle shorted proportionately less at higher torques. This may be due to a slight change in tendon compliance as the muscle contracts harder but we cannot further substantiate these ideas. We used torque as a reference value as it has been shown that under isometric conditions for relatively small fluctuations, torque varies linearly with small changes in muscle length (Loram *et al.*, 2007). However this is not a perfect validation technique because torque can only serve as a proxy for muscle length and we have no way of knowing the true values. These results show the extent of muscle shortening in a so-called isometric effort and they also provide further evidence that muscle length changes can provide a very useful indication of muscle activation as an alternative to rectified surface EMG. In the slow ramp task, for a 1 Nm increase in torque, the calculated shortening in muscle length was 143 ± 0.012 µm, whereas in the saw tooth task it was 116 ± 0.006 µm. Again, it is possible this can be explained by a difference in tendon compliance between the two conditions (sawtooth vs ramp) but these ideas require further investigation.

As we had no method of measuring accuracy, we compared our offline arterial diameter measurements with those of an existing technique. The similar diameter change, and more consistent signal from measurements at rest, suggests that the software is providing a

reasonable estimate of arterial diameter. Fig. 5A (online technique) shows considerably more variation between cardiac cycles (mean SD = 0.31 %) than Fig. 5B (using Mocha - mean SD = 0.09%). Tracking arterial diameter using a cross sectional view (Fig. 5C) was also possible and resulted in a similar diameter change, though a rather different profile. The technique was also possible during exercise where contraction of the muscle causes large movements of the vessel under observation (see supplementary video 2), presenting insurmountable problems to existing tracking programmes. Here, the technique is tracking large translations and distortions (changes in diameter) of the artery simultaneously. These observations, suggest potential for measures of arterial diameter in circumstances not previously possible.

Conclusions

This new method is a significant step forward in offline tracking. Planar tracking is successful in following the simultaneous translation and distortion of objects in low quality images. The software is inexpensive, requires minimal technical skill, and no programming knowledge. The only shortcoming is a small drift (common to all frame by frame trackers) which means that the low frequency components of tracker outputs must be interpreted with caution. Our simple biological experiments illustrate that the technique is flexible and not confined to one task. The results that have been described involve ultrasound analysis, but the technique shows promise in analysing body sway, movement of limbs in movement disorders such as tremor, tracking behavioural changes in animals and may find many other applications.

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Chapter 3

SLOW PLATFORM TILTS REVEAL A HIGH SENSITIVITY CONTROL PROCESS IN QUIET HUMAN STANDING

ABSTRACT

Sensory thresholds in human standing have often been investigated using psychophysical methods. There are few data describing the size of disturbance required to evoke a neural response. To investigate this, we applied a slow constant velocity tilt (0.05°/s) to the support surface of standing subjects and used surface EMG and dynamic ultrasound imaging to measure reactive muscle responses. We used an automatic tracking method to extract muscle length data from the ultrasound videos. We found statistically significant changes ($p < 0.05$) in medial gastrocnmius EMG, soleus EMG, and soleus muscle length after 290 ms, 460 ms and 660 ms respectively. The muscle length and EMG data were in good agreement. The responses occurred when ankle angle and velocity were well below the size of consciously perceptible sway. These observations suggest that at least part of the balance control system is concerned with regulating ankle angle or tension with a very low threshold mechanism.

Introduction

Researchers are interested in the mechanisms of human balance control for a wide variety of reasons from the development of novel control paradigms (Peterka, 2003; Bottaro *et al.*, 2008; Gawthrop *et al.*, 2011), to the diagnosis and treatment of balance disorders (Mergner, 2010). Despite this, the process is still not fully understood. One intriguing aspect of balance control concerns the sensitivity with which the nervous system is able to detect and respond to unexpected disturbances. Knowledge of sensory thresholds is important because it has implications for our understanding of the mechanisms of balance control (Loram *et al.*, 2009*a*). If sensory thresholds are large, then neural control cannot correct for small sub-threshold disturbances, and may not be relevant to the small sways observed during quiet standing. However, if sensory thresholds are very small, neural control may be pervasive throughout standing balance control.

A number of authors have investigated the sensory thresholds of the balance control system by applying subtle perturbations to standing subjects, and using conscious perception of the perturbation as a criterion for stimulus detection. This provides important insights as to when subjects may consciously produce a control action to correct for a disturbance. Teasdale *et al.*, (1999) investigated subjects' detection of slow support surface tilts when standing with eyes closed. They found that, on average, slow tilts (0.01, 0.03, and 0.05 °/s) in the anterior-posterior plane were not reliably detected until the platform had rotated by approximately 1.7 ° irrespective of tilt velocity. In these experiments the axis of rotation was 1 m above the platform and consequently did not rotate the body through the axis of a specific joint. Maurer *et al.*, (2006) found a smaller threshold for reliable detection of platform tilts when rotating the support surface around the axis of the ankle joints. The

authors estimated a position detection threshold of 0.122° and a velocity detection threshold of 0.099°/s. Fitzpatrick and McCloskey (1994) used a different approach by asking subjects to report detection of anterior-posterior sways but did not require subjects to distinguish between movements induced by a small perturbation and those of normal body sway. With these methods, subjects could reliably perceive anterior-posterior sways of 0.06 to 0.12° when respective sway velocities were 0.13 to 0.043 °/s. This level of detection remained largely unchanged when both visual and vestibular inputs were excluded suggesting proprioceptive information is particularly important for sway detection.

Other experiments have focussed not on conscious detection, but on measuring the passive mechanical consequences, and active neural responses to slow perturbations. Gurfinkel *et al.*, (1995) described the reactions of standing human subjects to slow tilts of the support surface. Subjects with occluded vision stood quietly on a platform that was tilted forwards or backwards in the anterior-posterior plane. Averaged records showed that a ramp perturbation, consisting of a static period followed by a constant velocity tilt of 0.05°/s, initially resulted in a relatively fast inclination of the body in the direction of the tilt. After a period of around 3-5 seconds, the body 'braked' and the speed of the initial inclination then quickly decreased. The authors attributed this braking of the body to an intervention from the nervous system in a process that was normally dominated by passive control. In this control paradigm, neural detection thresholds can be relatively large because the body is passively stabilised for small sways by the short range stiffness of muscle (Rack & Westbury, 1974). However, it is now known that ankle stiffness alone is insufficient to provide stable human standing (Loram & Lakie, 2002*b*; Casadio *et al.*, 2005). Even under normal standing conditions on an unmoving support surface, the human body is unstable and requires

sustained active control to prevent collapse. It is therefore unlikely that the observed braking of the body observed by Gurfinkel *et al.*, (1995) represented a minimum neural threshold.

Indeed, other experiments include data that appear to suggest that the nervous system is highly sensitive to very small disturbances during standing. Fitzpatrick and Taylor (1992) investigated subjects' responses to imperceptible perturbations during quiet stance. Subjects stood quietly with their eyes closed while a servo motor slowly pulled them forwards via a weak spring attached to the their waist. The authors showed that averaged soleus EMG increased rapidly in response to the perturbations even before subjects were able to perceive their own sway, although it is difficult to determine precisely when this response occurred (see their Fig 6B). Indeed, it is very challenging to establish when the nervous system responds to such small stimuli with certainty because responses are small and difficult to confidently distinguish from ongoing background activity.

The purpose of these experiments was to resolve more precisely the sensitivity of the neural balance control system. We apply super slow support surface tilts to standing subjects, as done by Gurfinkel *et al.*, (1995) and use signal averaging to extract any small responses from the large background variation. To increase our confidence in our findings, we apply two independent techniques to measure muscle responses. Firstly, we use surface EMG to detect neural changes in muscles of interest. Secondly, we use dynamic ultrasonography in combination with an automated tracking method that allows us to measure tiny muscle movements (Osborne & Lakie, 2011). This tracking method is particularly suitable for the task because it has an excellent signal to noise ratio and, compared with many other tracking methods, is time efficient so that many trials may be analysed for subsequent

averaging. With this approach we attempt to uncover even very small early responses to rotations of the support surface.

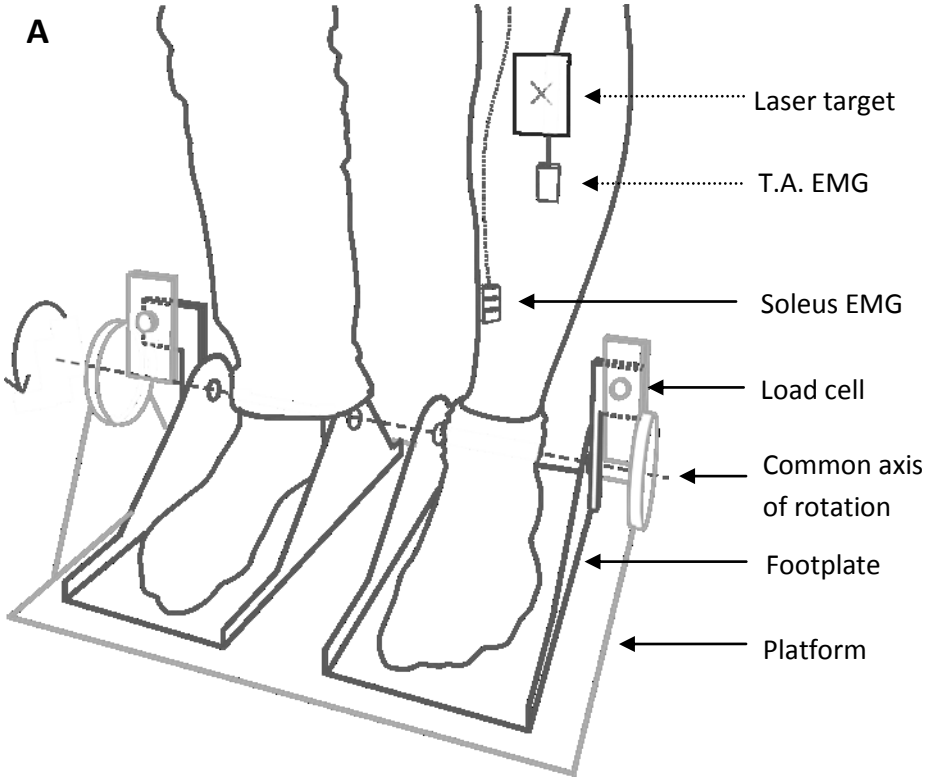
Methods

Subjects and ethical approval

Ten healthy people (6 male) aged between 20 and 57 took part in this study. The subjects gave written informed consent, and the study was approved by the local human ethic committee and conformed to the principles of the Declaration of Helsinki. One subject was omitted from analysis due to poor quality ultrasound images.

Experimental setup

Subjects stood upright on two custom built footplates with their feet aligned and approximately 30 cm apart (Fig. 1A). A servo motor controlled the position of a platform which in turn rotated the footplates around the axis of the ankle joint. Footplate angle was measured via a Hall effect precision potentiometer (CP 2UTX, Midori Precision Ltd, Japan). Changes in body angle were estimated from the horizontal displacement of the left shin. This was recorded by a laser range finder (Wenglor Sensoric, Germany) reflected off a flat white target secured slightly laterally to the tibia on the left leg (Fig. 1A – Laser target). Ankle torque was recorded from each leg by two horizontally mounted load cells (Sensotec model 31, Sensotect Inc., USA) which coupled the rotated platform to the footplates. Surface EMG (Delsys Bagnoli system) was recorded from the tibialis anterior (Fig. 1A), soleus, and medial gastrocnemius (Fig. 1B) muscles of the left leg. An ultrasound probe (5-10 MHz, DIASUS) was placed in a vertical plane over the medial gastrocnemius of the left leg, perpendicular to the skin (Fig 1B). In this position, the probe provided a longitudinal



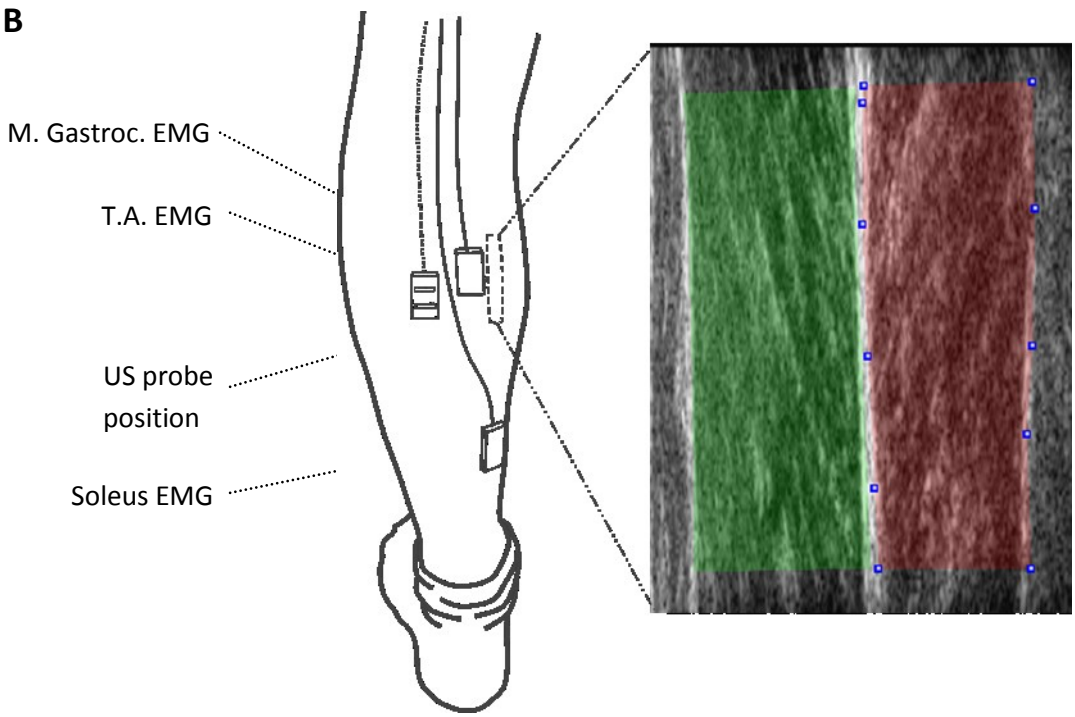


Figure 1. Experimental setup. Details on next page.

A, Setup for experiment 1. The subject stood relaxed on custom built footplates. A single servo motor controlled the angular position of the platform which in turn rotated the footplates around a common axis through the ankle joints. The diagram shows positioning of surface EMG electrodes and of the white reflective target used in combination with laser rangefinder to estimate shin angle. Further white reflective targets were placed on the thigh, chest and head (not shown). The laser rangefinders are also not shown but were reflected off the centre of each of the white targets (shown by the 'X'). **B**, Additions to setup for experiment 2. In experiment 2, subjects were stood on the same apparatus used in experiment 1 but this has been omitted for clarity. Diagram shows positioning of surface EMG electrodes and of the ultrasound probe (labelled 'US probe position'). An example of an image obtained with the ultrasound probe is shown on the right of the diagram. The sonograph shows a longitudinal section of the left calf muscle. The medial gastrocnemius is highlighted in green and the soleus is highlighted in red. The coloured highlighted sections show the area used by the automatic tracking technique to estimate changes in length of each muscle.

view of the pennate structure of both the medial gastrocnemius and soleus muscles. Ultrasound videos (pixel dimensions 137 µm x 137 µm) were captured at 15 frames/s and stored for subsequent analysis.

Experimental Protocol

During each trial subjects were asked to stand quietly with their eyes closed. We asked subjects to stand with eyes closed because psychophysical data has shown proprioceptive inputs to be particularly important in disturbance detection and we wanted to isolate this (Fitzpatrick & McCloskey, 1994). Subjects were able to relax between trials by leaning on a cushion behind them. At least one five minute break where the subject fully dismounted the apparatus was enforced in each experiment. Each trial consisted of one static period of no platform movement followed by either a toes-up or toes-down platform tilt. The static period lasted between 10 and 15 seconds (randomly determined), and the direction of the ramp was also randomly decided. The platform was tilted at a constant velocity (0.05 °/s) for 10 seconds (amplitude 0.5°) before the platform was returned to its original position and the trial ended. We chose this platform velocity because previous experiments by Gurfinkel *et al* (1995) showed that these tilts were not consciously detectible. We limited the ramp to ten seconds because we are most interested in the initial neural response. An ultrasound video was automatically triggered to begin recording 2.5 seconds prior to the platform movement onset and continued recording for a total of 10 seconds. Each subject completed 20 toes-up tilts and 20 toes-down tilts.

Additional experiments

In a supplementary experiment, we aimed to measure angles of different body segments in the sagital plane during the platform tilts.

Ten healthy volunteers (6 male), aged between 20 and 57 gave written informed consent to take part in the study. Three participants had also taken part in the previous experiments. The study was approved by the local human ethics committee and conformed to the principles of the Declaration of Helsinki.

The experimental protocol was identical to that described above with the omission of the ultrasound setup and the medial gastrocnemius EMG recordings, and with the addition of three laser range finders. Body segment angles were estimated from horizontal displacements of the shin (as above), thigh (belly of rectus femorus on the left leg), chest (centre of sternum) and head (centre of forehead). Horizontal displacements were measured by four laser range finders (Wenglor Sensoric, Germany) which were reflected off a flat white target secured to each anatomical location.

Signal measurement and recording

All data were recorded using a data acquisition card (NI PCI-6229) in combination with MATLAB (Data acquisition toolbox, Mathworks, 2007b). Data were analysed in custom written scripts using MATLAB. Signals recorded from the laser rangefinder and load cells were lowpass filtered (8 Hz cut off). Torque data from the left ankle is presented throughout the paper.

Data averaging

Each individual trial differed in length because the length of the static periods preceding ramp movements was randomly determined. To align each trial, data were time locked around the signal commanding the onset of platform movement. We also chose to combine tilts of both directions into a single average. This was justified on the grounds that we were looking at a very small response buried in much larger background noise. As the response to the perturbation was found to be effectively equal and opposite in both directions (the correlation between the mean toes-down and toes-up ankle angle data was $r = -0.99$), we reversed the polarity of the toes-up tilts and combined them with the toes-down tilts. This method makes best use of all the data, in particular the technically challenging analysis of ultrasound videos.

EMG analysis

All EMG data were bandpass filtered between 60 and 500 Hz, rectified and then integrated with a time constant of 50 ms before being downsampled to 100 Hz. Individual subjects' EMG was then averaged. Each individual subject mean was then scaled to its maximum range so that the maximum value was 1, and the minimum value 0. This was an important step in the analysis to account for the large variability of EMG signal sizes between subjects. Performing this step stopped subjects with large EMG signals dominating the mean and substantially improved the correlation between the median and then mean (with $r^2 = 0.99$, without $r^2 = 0.79$).

Soleus EMG was measured in 9 subjects in the initial experiment, and a further 10 subjects in the additional experiments. To make best use of the soleus EMG, we pooled these data and present them together in the group average.

Automatic tracking of dynamic ultrasound videos

We used commercially available automatic tracking software (*Mocha for After Effects V 2.6 – Imagineer Systems*) to analyse the ultrasound videos collected in experiment 2. The general principles of this technique have been described elsewhere (Osborne & Lakie, 2011). To track length changes of soleus and medial gastrocnemius muscles, a spline was manually drawn around the edge of each muscle to determine the search region used by the tracker to estimate changes in muscle length. An example of this is shown in Figure 1B (green and red areas in the sonograph). Each video was then automatically tracked. The tracker works on a frame by frame basis and changes the shape of the spline to match the change in shape of the muscle. Following the automatic tracking, the quality of each track was checked by visual inspection and, where necessary, further automatic refinements were made - predominantly to correct for low frequency drift. Tracking data was saved and then imported in to a custom written MATLAB script which decoded the file data and returned a muscle length change in units of pixels. The output of each track was based on the relative movement between the proximal and distal aponeurosis of each muscle. This method eliminates the effect of any movement between the ultrasound probe and the skin. The tracking output was then multiplied by a calibration factor (each pixel constituted 138 μm) to provide an estimate of muscle length change in millimetres for each muscle and each trial. In total, 360 ultrasound videos were analysed. For these small length changes we assume that changes in fascicle length and changes in muscle length are linearly related.

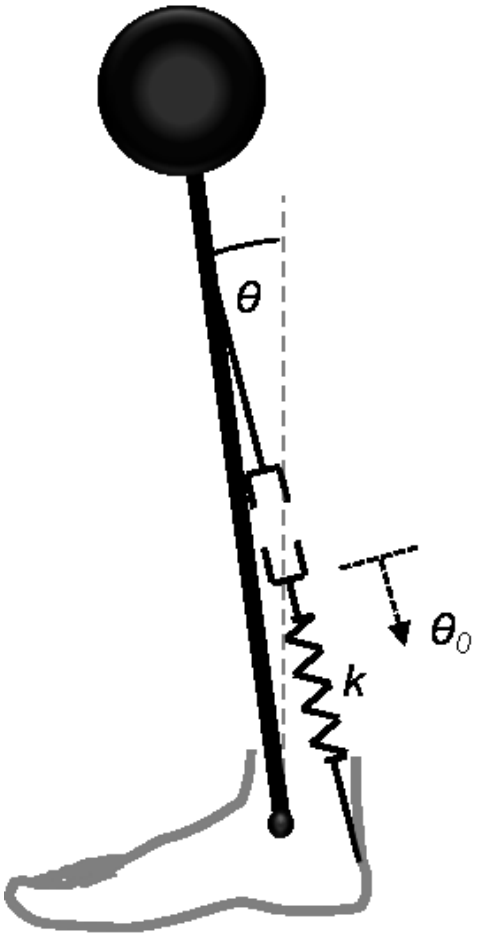


Figure 2. Inverted pendulum model of human standing.

Torque is modulated by length changes of the spring like element with stiffness *k* (the achillies tendon). The length of the tendon is determined by θ (ankle angle), or θ_0 (calf muscle length).

Estimating torque from muscle length and ankle angle data

In a simplified model of human standing the body may be represented as a single link inverted pendulum that sways in the anterior-posterior plane about the axis of the ankle joint (Fig 2). The body tends to topple forward and is prevented from falling by restoring torques. In this model an increase in torque can be produced by an increase in θ (a forward lean of the body), or by a decrease in θ_0 (a contraction of the calf muscles). In both cases, there is a change in length of a spring-like element with stiffness *k* (the achilles tendon). Thus, torque may be calculated as follows:

$$T_{est} = k(\theta - \theta_0)$$

where T_{est} is our calculated estimate of torque, θ is ankle angle, θ_0 is the length of the contractile portion in angular terms, and *k* is the angular stiffness of the spring-like component. In these experiments we have independently measured actual torque *(T)*, ankle angle *(θ)* and muscle length change *(θ_0)*. If our measurements of θ and θ_0 are accurate, a simple scaling of *k* should mean that T_{est} is a good estimate of *T.* We are confident that our measure of θ is accurate because it is measured using a laser range finder. Our measure of θ_0 is more technically difficult and an independent verification of the accuracy of the technique is useful. Thus, our comparison of *T* with T_{est} allows us to validate our measurements of θ_0.

Where units of muscle length are converted into angular units ($L = MA \sin(\theta_0)$, *L* = muscle length, *MA* = moment arm), we assume an achilles tendon moment arm of 5 cm (Maganaris *et al.*, 2000*b*).

Results

Figure 3 shows the group mean result ± 95 % confidence intervals. The polarity of data from toes-up tilts has been reversed and averaged together with toes-down tilts and so data in the figure may be interpreted in the context of a toes-down tilt (see methods).

At time zero (vertical dashed line), when the platform movement was commanded to begin, the velocity of the ramp rose sharply (Fig 3A – light grey trace), and the platform began to tilt forwards (Fig 3A dark trace). As the platform began to move, there was a small decrease in ankle angle (Fig 3B, dark trace marked 'a') which followed a decrease in ankle velocity (Fig 3B light trace). At this time, the ankle was being moved into plantar flexion by the platform rotation while the body was maintaining its position in space. This slight plantar flexion of the ankle was accompanied by a synchronous reduction in torque (Fig 3C). If the torque reduction was purely a mechanical consequence of the ankle plantar flexion, and there was no change in neural drive to the calf muscles, we would predict that the soleus and gastrocnemius muscles would slightly shorten here. However, Fig 3D shows that there was a slight lengthening of soleus (dark trace) and medial gastrocnemius (light trace). To test this statistically, we performed a two-tailed one sample t-test at each time point on the muscle length data to determine whether muscle length significantly deviated from zero (note that for presentational purposes the medial gastrocnemius trace is offset from zero). The resulting p-values from each test are plotted over time in Fig 3E (dark line for soleus and light grey line for medial gastrocnemius). The horizontal black line in the plot shows where p = 0.05. During the baseline period (from -2 to 0 seconds), neither muscle length deviated significantly from zero. However, 660 ms after time zero, the soleus muscle showed a

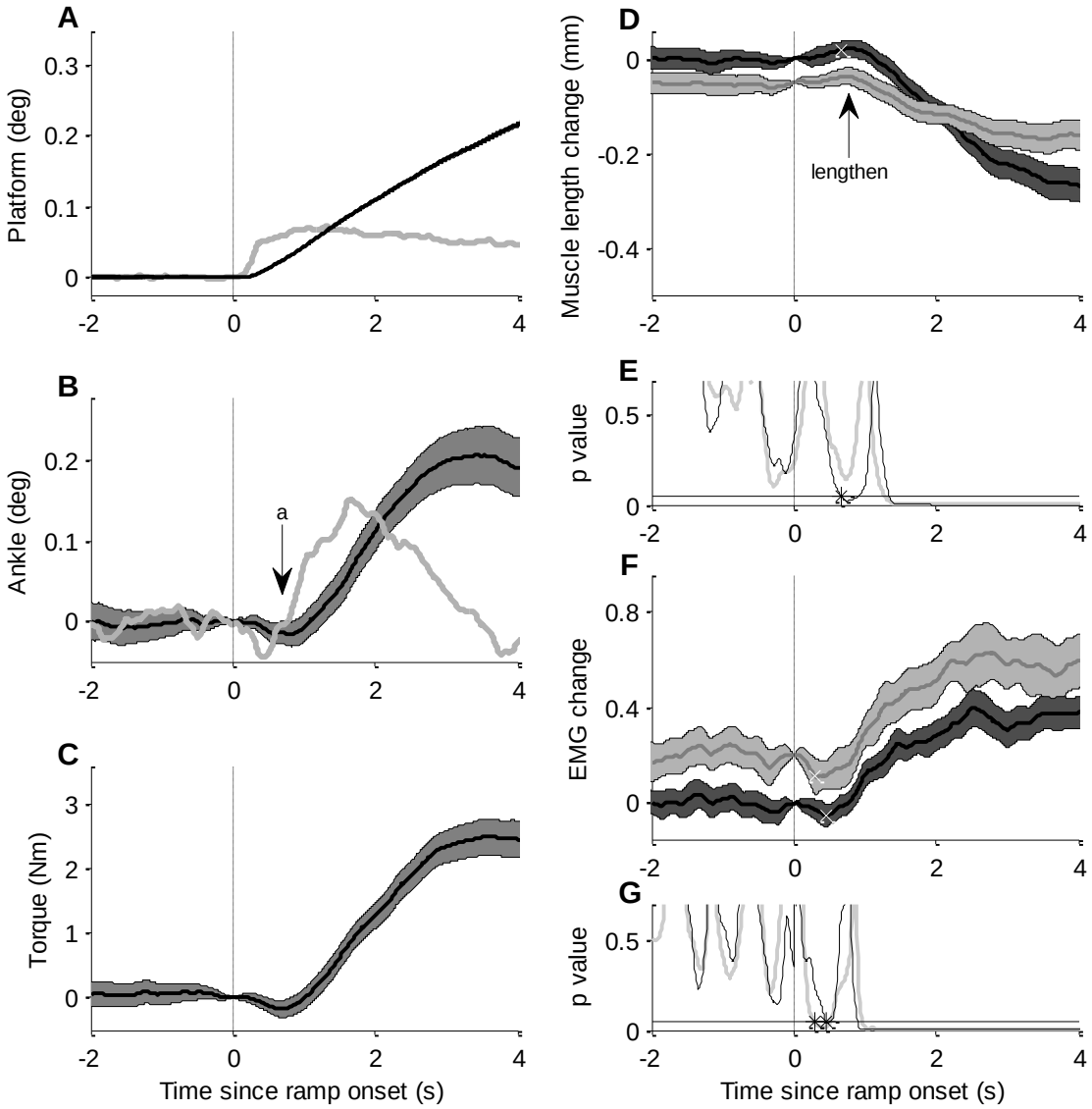


Figure 3. Averaged results from all subjects.

The polarity of the toes-up tilt has been reversed and averaged together with the toes-down tilt to encompass all data. Time zero, marked by the vertical line, denotes the start of the perturbation. In each plot, the thick line shows the mean and the shaded area shows the 95 % confidence limits. A, platform angle (dark trace) and platform velocity (°/s) (light trace); B, change in ankle angle (dark trace) and ankle velocity (°/s) (light trace); C, change in torque; D, change in muscle length for Soleus (dark trace), and Medial Gastrocnemius (light grey trace); E shows, for each time point, the statistical probability that the muscle length data is different from zero by chance for Soleus (dark line) and Medial Gastrocnemius (light line) F, change in surface EMG for Soleus (dark trace) and Medial Gastrocnemius. G, as plot E but for surface EMG

significant lengthening response ($p < 0.05$, marked by the white cross in Fig 3D, and black asterisk in Fig 3E). However, the small lengthening response of the medial gastrocnemius did not reach statistical significance ($p = 0.15$). To cross check the muscle length data, we can examine the corresponding EMG data for agreement. This is shown in Figs 3F and 3G. Again, neither trace significantly deviated from zero during the baseline period (from -2 to 0 seconds). However, after the start of the perturbation there was a slight reduction in mean EMG in both the soleus (dark trace) and medial gastrocnemius EMG (light trace – again this has been offset from zero for clarity). This initial reduction reached statistical significance in the soleus EMG after 460 ms and after 290 ms in the medial gastrocnemius EMG (see Fig 3F white crosses and Fig 3G black asterisks). Thus, during the first second following the start of the perturbation, a small ankle planter flexion appears to have been accompanied by a neural response that is visible in both the muscle length data and the EMG.

A breakdown of these three statistically significant observations (soleus muscle lengthening and soleus and medial gastrocnemius EMG reduction) is shown in table 1. This shows the largest absolute value of each variable (e.g. platform angle, ankle angle etc) that occurred from time zero up until the point of statistical significance of each observation.

After this initial period the response was characterised by a rapid lean of the body in the direction of the platform tilt. This is visible after approximately 1 second as an abrupt increase in ankle angle (Fig 3B) which may be interpreted as a forward sway of the body. This was clearly accompanied by the following: 1) an increase in torque (Fig 3C); 2) a shortening of soleus, and to a lesser extent medial gastrocnemius (Fig 3D); 3) a rise in EMG in both soleus and medial gastrocnemius (Fig 3F).

	M. Gastroc. EMG response (290 ms)	Soleus EMG response (460 ms)	Soleus muscle length response (660 ms)
Platform angle (°)	0.0024	0.011	0.022
Platform velocity (°/s)	0.035	0.052	0.058
Ankle angle (°)	-0.0017	-0.0094	-0.015
Ankle velocity (°/s)	-0.023	-0.044	-0.044
Torque (Nm)	-0.021	-0.092	-0.17

Table 1. The maximum absolute value of each variable achieved between time zero and each response.

Further analysis

In the initial phase of the response (0 – 1 second) we observed very small changes in muscle length and EMG. To increase confidence in the data, we chose to perform some further analysis which is shown in figure 4.

Figure 4A shows the first 1.75 seconds following the onset of the perturbation. Three traces are shown: 1) ankle angle (light grey full line), 2) left leg measured torque divided by calculated angular stiffness (T/k) giving a quantity in units of degrees (dark grey thin line), and 3) left leg estimated torque divided by calculated stiffness (T_{est}/ k) also giving a quantity in units of degrees (dark grey dashed line). Estimated torque (T_{est}) is calculated from changes in muscle length and ankle angle (see Fig 2 and methods for details). The decrease in ankle angle alone (light grey full line) is insufficient to account for the total torque change (dark grey full line). A more convincing qualitative explanation of the torque change is shown by estimated torque (T_{est}) which accounts for both ankle angle and muscle length changes (dashed grey line).

Figure 4B shows the angle of different body segments over the first 1.75 seconds of the perturbation. These data were obtained from ten subjects in additional experiments. Each line represents the angle of a different body segment with respect to the platform. In order of darkness (shin angle is the lightest trace), the figures shows: shin angle, thigh angle, chest angle and head angle. If the body behaved exactly like an inverted pendulum, all four lines would perfectly overlap. This is clearly not exactly the case, but the differences between body segments are very small. In particular, the two lightest traces (the shin and thigh)

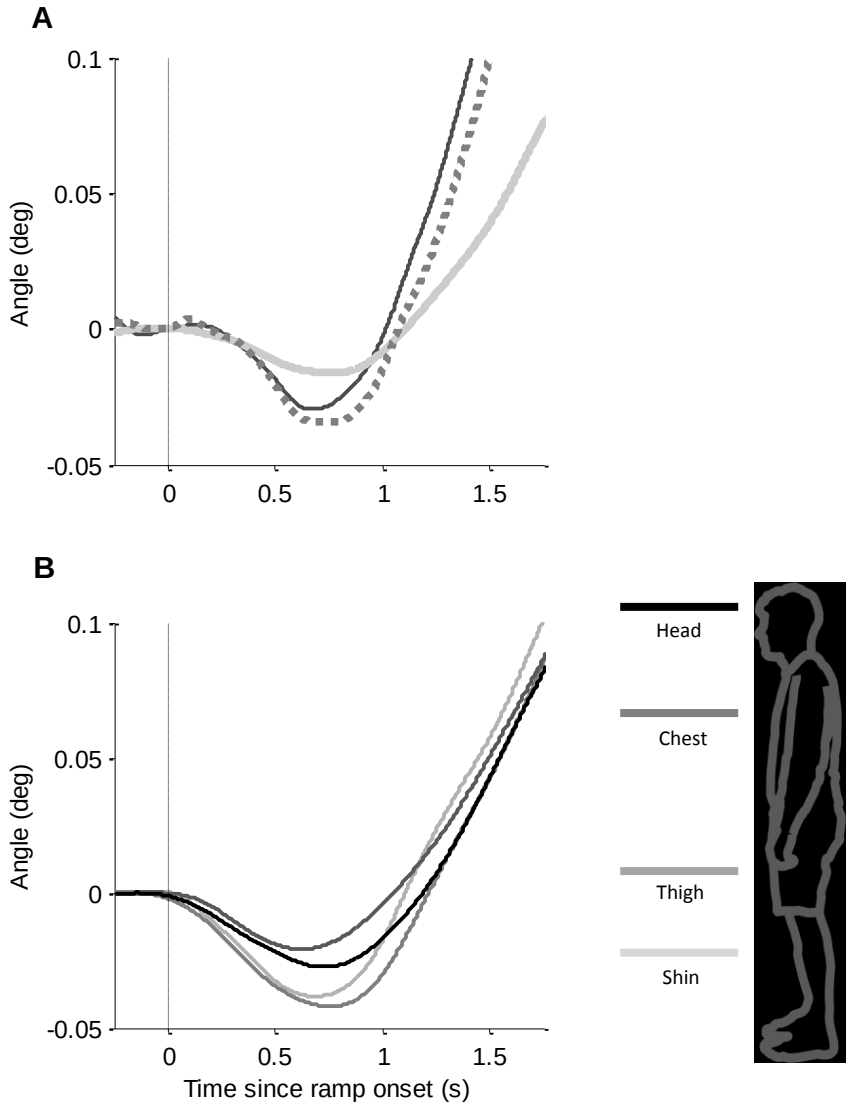


Figure 4. Initial response to slow ramp tilt.

A, The thick light grey line shows the change in ankle angle for the first 1.75 seconds following the onset of ramp movement. The thin dark line shows a plot of left leg torque (Nm) divided by calculated angular stiffness (Nm/deg) giving a quantity in units of degrees. The thick dashed grey shows the sum of ankle angle and soleus muscle length changes (where muscle length changes have been converted to angular units). This is an independent estimation of the quantity shown in the dark grey line (see methods). B, shows the change in angle of different body segments (data gained from additional experiments).

decrease more than the two darker traces (the chest and head) which means the body leant forward slightly at the hips.

Discussion

The results of these experiments describe the initial response of standing human subjects to super slow tilts of the support surface. We have used dynamic ultrasonography and EMG to reveal a small neural response to a tiny unpredictable perturbation. This suggests that the nervous system may be highly sensitive to small disturbances during unperturbed standing. In the following discussion we examine the evidence for this interpretation of the data. Throughout the discussion we refer to the tilt and subsequent response in the context of a toes-down tilt for clarity and for consistency with figures. However, a toes-up tilt resulted in a very similar equal and opposite response in all variables.

Figure 3B shows that soon after the start of the platform rotation we observed a decrease in ankle angle (Fig 3B, marked 'a'). This observation is predictable with a simple mechanical model. As the platform begins to move the toes down, the moment of inertia of the body prevents it from immediately toppling over. This means that the ankles are momentarily moved into plantar flexion while the body takes time to accelerate forwards. Accompanying the decrease in ankle angle was a synchronous reduction in torque (Fig 3C). Again, some reduction in torque would be predicted on mechanical grounds. In a simple model, where torque is modulated by changes in ankle angle and calf muscle length (Fig 2), a reduction in ankle angle produces a reduction in torque even in the absence of any neural modulation. However, the records of muscle length and EMG (Fig 3, panels D and F) suggest that, even at this early stage, the nervous system also contributed to this torque reduction. Figure 3D shows that on average the soleus muscle (dark trace) lengthened very slightly (≈ 20 μm) as

the torque reduced. Mechanics demand that a lengthening of soleus at this time is only possible under control of the nervous system. If, as is the case here, the ankle is being moved into plantar flexion, the soleus muscle cannot lengthen on purely mechanical grounds: it can only do so because of a reduction in neural drive. The corresponding EMG record (Fig 3F, dark trace) shows a small (relative change ≈ 5 %) but significant reduction in soleus EMG just prior to the soleus muscle lengthening. We also observed a slight lengthening in the medial gastrocnemius muscle at this time (Fig 3D, light trace) although this did not reach statistical significance. However, there was a significant reduction in medial gastrocnemius EMG (Fig 3F, light trace) which suggests the observed muscle lengthening may have been genuine.

These simple observations suggest that the nervous system responded with great sensitivity. Table 1 shows that all three responses occurred when platform/ankle angle and velocity were well below the size of even the smallest consciously perceptible sways (Fitzpatrick & McCloskey, 1994; Maurer *et al.*, 2006*b*). These observations appear broadly consistent with data from a previous experiment where soleus EMG was shown to rise in response to a small torque perturbation (Fitzpatrick & Taylor, 1992). The strength of the present study is that we are able to define the start of the response with much greater certainly because we have measured the muscle behaviour with two independent methods.

We aim to test our interpretation of the data by addressing the following questions: 1) Are the muscle length data reliable? 2) Is the neural response a direct consequence of the platform rotation or could it be attributed to something else? 3) Does this response make functional sense?

Are the muscle length data reliable?

Figure 4A estimates the contributions of ankle angle change and soleus muscle length change to left leg torque modulation within the first 1.75 seconds of the platform tilt. To allow for direct comparison, torque values are plotted in angular units by dividing by the estimated angular stiffness (*k*) (see methods for details). The contribution of ankle angle change to total torque change is shown simply by the change in ankle angle (light grey line). This may be compared with the total torque change (*T/k*) which is shown by the dark grey thin line. If ankle angle were the only contributing factor to ankle torque changes, these two lines would be identical (assuming measurements of both variables were perfectly accurate). Clearly, the change in ankle angle is not the only contributing factor to the change in torque. The logical conclusion is that there is also a change in calf muscle length. We are able to examine the contribution of calf muscle length change because we have measured this by automatically tracking ultrasound videos. The grey dashed line in Fig 4A shows the sum of soleus length change (in angular units) and ankle angle change which equates to the variable T_{est}/k. This is qualitatively a good match for *T/k* (dark grey line). Therefore, the best match to the independently measured torque trace is achieved when accounting for both ankle angle and muscle length which suggests that the observed change in muscle length is reliable.

Is the neural response a direct consequence of the platform perturbation or could it be attributed to something else?

We wished to examine the possibility this early neural response was related to a systematic postural adjustment that was not a direct consequence of the ankle plantar flexion. In this case, we would assume the reaction was a genuine response, but one that departed from the normal 'ankle strategy' strategy of control (Winter *et al.*, 1998). Figure 4B shows the

angles of the shin, thigh, chest and head relative to the angle of the support surface. If the body were to behave as a perfectly rigid inverted pendulum, all traces would be indistinguishable. Although the agreement of all body segments is strong, the chest and head angles do not quite decrease to the same extent as the shin and thigh. This means that the body is bending forward slightly at the hips. This movement of the upper body will move the centre of mass slightly further forward, and, if anything, only exacerbate the need for a calf muscle contraction to increase ankle torque. Again, this is the opposite of what we observe as the calf muscles lengthen at this time. Thus we conclude that any non-inverted pendulum like behaviour does not provide a satisfactory explanation for the observed change in soleus length.

Is it possible that the response was somehow anticipatory rather than reactive? Schweigart and Mergner (2008) found that subjects anticipated similar platform tilts by leaning forward slightly prior to the onset of the perturbation. The authors attributed this to the body moving itself into a more optimal range for working balance in anticipation of a disturbance. We can discount this phenomenon in the current experiment for two reasons. Firstly, in the present experiments, subjects did not know when the platform would start moving - the onset of the tilt was randomly determined within a 5 second window. In the experiment by Schweigart and Mergner the great majority of trials were purposefully started with a consistent delay of 4 seconds meaning subjects could learn to anticipate the onset of platform movement. Secondly, in the present experiments subjects had no prior knowledge of the direction of the tilt and yet the response we observed was approximately equal and opposite in both directions. This contrasts with the anticipatory response reported by Schweigart and Mergner which was a consistent forward lean irrespective of the tilt

direction. For the same reason, we can discount the possibility that subjects were reacting to an unintended stimulus related to the onset of platform movement as opposed to the ankle rotation itself.

Does this response make functional sense?

At first, this response by the nervous system seems counterintuitive. A platform rotation that leads to a mechanical reduction in ankle torque will result in the body toppling forwards. To counteract this, the nervous system would need to contract the calf muscles to increase ankle torque (Loram *et al.*, 2004, 2009*d*). Instead we have observed a reduction in neural drive and a lengthening of the calf muscles which exacerbates the torque deficit and most likely contributes to the subsequent large forward sway of the body (Fig 3B 1 – 3 seconds). This intriguing observation may be better understood in the context of unperturbed standing. On an unmoving support surface, the same ankle angle change could only occur if the body were to sway backwards. In this situation, the nervous system is required to reduce ankle torque to prevent the body from swaying further backwards. The solution is to lengthen the calf muscles: exactly the response we have observed. As the ground is normally static, these observations make perfect functional sense if the threshold of detection is very low.

This suggests that at least part of the balance control system is concerned with actively maintaining either ankle angle or ankle tension with a very low threshold mechanism. We speculate that afferents located in the lower legs and feet are the most likely candidates for disturbance detection at this level. We can discount visual information because the experiments were conducted with eyes closed. Detection by the vestibule can also be ruled out: if the gravicentric vestibular signal was dominating, we would not expect the nervous

system to misinterpret a rotation of the ankles as a body sway. Thus we suggest that sensors located in the lower legs or structures of the foot that detect position, movement, or force, are the most likely candidates. Muscle spindles are traditionally thought to be important contributors to the sensation of joint angle and velocity (Matthews, 1981; Gandevia *et al.*, 1992; Proske, 2006). However, experimental (Loram *et al.*, 2007*a*, 2007*b*) and theoretical studies (Loram *et al.*, 2009*c*) have shown that, during normal human stance where typical sway size is 0.13 deg (Loram *et al.*, 2005*c*), the soleus and gastrocnemius muscles are 10 – 15 times stiffer than the Achilles tendon due to short range muscle stiffness (Hill, 1968; Rack & Westbury, 1974; Campbell & Lakie, 1998). Consequently, active fluctuations in extrafusal muscle length are one order of magnitude higher than passively transmitted contributions. This is likely to reduce the accuracy of a (theoretically possible) rigid α – γ linkage that works to subtract active fluctuations from the afferent signal. A more robust detection of passively transmitted ankle joint rotations could come from a muscle that is predominantly passive during standing such as the tibialis anterior (Di Giulio *et al.*, 2009). Additionally, force sensitive afferents such as Golgi tendon organs may also contribute to the sense of joint rotation even in passive muscle (Gregory & Brockett, 2004). Force sensing afferents have the added advantage that when, as in quiet standing, the ratio of muscle to tendon stiffness is high, they are not subject to the same mechanical transmission limitations as muscle spindles (Loram *et al.*, 2009*c*). It is known that force information can be used to aid stability during postural control (Prochazka *et al.*, 1997), and intriguingly, one author has found that the inclusion of a positive force feedback loop into their model of quiet standing improved the model fit to experimental data (Peterka, 2003). Another important factor may be sensors that detect deformations of the foot arch (Wright *et al.*, 2011).

Conclusions

In conclusion, we have observed a rapid neural response to a small, slow support surface tilt during quiet standing. These observations suggest that, despite complications of large ongoing background sway, and sensors that are confounded by active modulation, the proprioceptive afferents are highly sensitive to perturbations that are considerably smaller than normal sway size and below reported values of conscious detection.

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Chapter 4

REFLEX AND HIGHER LEVEL CONTROL IN HUMAN BALANCE

ABSTRACT

Many authors propose that the control of quiet standing is achieved primarily through reflex pathways while others favour an explanation that includes higher level control. To investigate these proposed mechanisms we compare two balance control tasks. In one task both local proprioceptive reflexes and higher level voluntary control may contribute to balance control, and in a separate task reflexes are excluded and only voluntary control is possible. In each task we used a novel paradigm to investigate the effect of altering the proprioceptive gain on task performance and control characteristics.

Subjects were strapped around the waist to a vertical backboard to eliminate their sway. They stood on two servo controlled footplates that could rotate around the axis of the ankle joints. With their eyes closed subjects balanced a virtual inverted pendulum that was matched to their own body characteristics. The angle of the virtual inverted pendulum was reflected in the angle of the footplates. We varied the gain between the sway of the pendulum and the rotation of the ankles. For 'physiological' gain (gain = 1), as the pendulum swayed forward by 1 degree, the subjects ankles were dorsi flexed by 1 degree. At a gain of 3, if the pendulum swayed forward by 1 degree, the subjects' ankles were dorsi flexed by 3 degrees. In all cases the torque required to stabilise the sway of the pendulum was identical: only the relationship between pendulum sway and ankle angle was changed. We varied the ‘proprioceptive gain’ between the following values: 0.3, 0.5, 1, 2 and 3. The

experiment consisted of two conditions: 1) Myoelectric balancing of the virtual inverted pendulum using the lower leg muscles (soleus and tibialis anterior); 2) Myoelectic balancing of the virtual inverted pendulum using the flexor and extensors of the wrist. Control with the lower leg muscles allowed for voluntary control and local reflex control as in normal standing. Control with the wrist allowed for voluntary control only. We also created a simple model of balance control that utilises both reflex (short delay) and higher level (long delay) feedback pathways.

In both conditions sway size and velocity of the inverted pendulum showed a systematic reduction as proprioceptive gain was increased. At equivalent gain settings sway size was smaller when myoelectric control derived from the leg muscles was used. This effect was particularly pronounced at higher gains.

Increasing the proprioceptive gain may mean that thresholds for detection of sway are attained more quickly permitting more rapid and effective corrective action. Control using leg muscles is superior either because myotatic reflexes make an additional stabilising contribution to control or because it is a more familiar task which subjects found easier to perform because sensation and the controlling muscles are co-localised. Simulations show that, in comparison to higher level feedback alone, control using a combination of reflex and higher level feedback is superior. This suggests that the experimental results (control with legs is superior to control with arms) may be explained by the additional stabilising contribution of reflex feedback.

Introduction

The control of human upright stance is achieved through both passive mechanical and active neural mechanisms. It is now well established that control by purely passive mechanisms is insufficient to stabilise the human body (Loram & Lakie, 2002*b*; Casadio *et al.*, 2005) due to the compliant achilles tendon (Loram *et al.*, 2007*b*). Thus active control by the nervous system is required for balance. In a simplified conception, active control of balance may proceed via two parallel control loops: peripheral reflexes and higher level voluntary pathways. Peripheral reflexes may be mediated by vestibular (Fitzpatrick *et al.*, 1994*a*; Runge *et al.*, 1998; Carpenter *et al.*, 2001) or proprioceptive (Nashner, 1976; Fitzpatrick *et al.*, 1992) afferents and are associated with minimal computation and short time delays. The penalty for minimal computation is that, in some circumstances, such reflexes can actually be destabilising (Nashner, 1976; Diener *et al.*, 1984; Loram & Lakie, 2002*b*). In contrast, higher level voluntary pathways are very flexible and difficult to deceive (less likely to produce an inappropriate response) but are associated with longer time delays.

The majority of researchers believe that quiet standing is dominated by reflex control. Perturbing human stance normally produces a fairly stereotyped sequence of corrective responses (Nashner, 1976; Diener *et al.*, 1984, 1985; Welch & Ting, 2008). Similar looking responses have also been observed in cats (Lockhart & Ting, 2007). Indeed, it is well known that such postural reactions are preserved in exaggerated form in the decerebrate cat (Bard & Macht, 1958). Many researchers believe that the solution to the problem of balance control is similar across different species and that access to higher level neural circuitry is not necessary to produce appropriate corrective responses (Deliagina *et al.*, 2007).

Other researchers have pointed to clear differences between the control of human upright stance and the control of quadrupeds such as cats. One major difference is that quadrupeds have a proportionally large base of support and low centre of gravity, whereas human bipedal stance has a small base of support and high centre of gravity. Therefore the problem of balance requires a refined solution in humans which is not necessarily the case in quadrupeds. Additionally, simple stretch reflex stabilisation may be all but ruled out in human balance control: low ankle stiffness means that the calf muscles, which are particularly crucial in normal stance control, contract rather than stretch when the body sways forwards (Loram *et al.*, 2004, 2005*b*, 2009*d*). This is crucial because it means that a simple measure of muscle length or velocity does provide the central nervous system with useful information about the position or velocity of the body. Furthermore, investigations into human manual balance control, which is an entirely voluntary task, have demonstrated some striking similarities to the control of quiet standing. Lakie and Loram (2006) asked subjects to balance their own body or a mechanically equivalent load (an unstable inverted pendulum) using a joystick. Peripheral reflexes could not contribute to balance because control was imparted through voluntary movements of the joystick based on visual feedback alone. Analysis revealed that sway size and sway duration in this task are very similar to the sway characteristics in normal standing. In addition, the mean duration of control actions is remarkably similar to the mean duration of calf muscle adjustments that occur during quiet standing (Loram *et al.*, 2005*c*). Lakie and Loram (2006) also showed that the rate of corrective action during manual balancing remains unaffected whether feedback is provided by visual, vestibular, or proprioceptive feedback either exclusively, or in different combinations.

The traditional reflex control paradigm has also been questioned because evidence has almost exclusively been gathered from perturbation experiments. Perturbation studies may be criticised on the grounds that they change the nature of the process that is being studied. Most perturbation studies use large platform displacements (0.5 – 8 deg) to produce reflex responses (Nashner, 1976; Diener *et al.*, 1984; Peterka, 2002; van der Kooij & de Vlugt, 2007; Welch & Ting, 2008). It is not clear that such responses should apply to the control of normal unperturbed standing where the average sway size is just over a tenth of a degree (Loram *et al.*, 2005*c*) which may be below the threshold of peripheral reflex mechanisms (Loram *et al.*, 2007*a*).

Here, we aim to investigate the contribution of both higher level voluntary, and proprioceptive reflex pathways to balance control. We asked subjects to balance an inverted pendulum using either the muscles of the leg or the muscles of the forearm. In both cases feedback of load angle was provided through rotation of the ankle joints (see Fig 1). Why did we choose these two balance tasks? Balance of an inverted pendulum using muscles of the legs has been studied quite extensively (Fitzpatrick *et al.*, 1992, 1994*b*; Loram *et al.*, 2001; Loram & Lakie, 2002*a*). This paradigm is a useful simplification of the normal standing process where the human body is replaced by an equivalent body (the inverted pendulum) and sway is restricted to a single plane around the axis of the ankle joints. Several authors have concluded that this simplified task is broadly equivalent to real standing (Fitzpatrick & Taylor, 1992; Fitzpatrick *et al.*, 1992; Fitzpatrick & McCloskey, 1994). Balance of the inverted pendulum using the muscles of the legs, like real standing, might be achieved through higher level control (Loram *et al.*, 2005*c*, 2009*d*), through reflex control (Fitzpatrick *et al.*, 1992; Lockhart & Ting, 2007; Welch & Ting, 2008), or through a combination of both. We

refer to this as the 'leg control' condition. We also wanted to study an equivalent task that excluded the possibility of reflex control. We did so by asking subjects to complete the same task but using their forearm muscles to balance the inverted pendulum. This is somewhat comparable to previous manual balance control experiments (Lakie *et al.*, 2003; Lakie & Loram, 2006). We refer to this as the 'arm control' condition. Thus we studied balance of an inverted pendulum under two conditions: control with the legs (where both reflex and higher level control is possible), and control with the arm (where only higher level control is possible). This enables a comparison of balance with, and without, reflex control loops.

We also aimed to manipulate the extent of reflex control by changing the peripheral proprioceptive gain using a novel paradigm. We anticipated that higher sensory gains, where afferent inputs are larger, would be more likely to elicit proprioceptive reflex responses. Thus, in the 'leg control' condition we predicted more reflex input at higher gains whereas in the 'arm control' condition there can be no reflex input irrespective of the proprioceptive gain. We compare balance performance between the two conditions and conclude that peripheral reflexes do contribute to human balancing of an inverted pendulum, but that control is dominated by higher level mechanisms. A simple feedback model of balance control demonstrates that our interpretation of the experimental results is plausible.

Methods

Subjects and Ethical approval

Six healthy people (all male) aged between 25 and 58 volunteered to take part in this study. All subjects gave written informed consent. The experiments were approved by the local ethics committee and conformed to the principles of the Declaration of Helsinki.

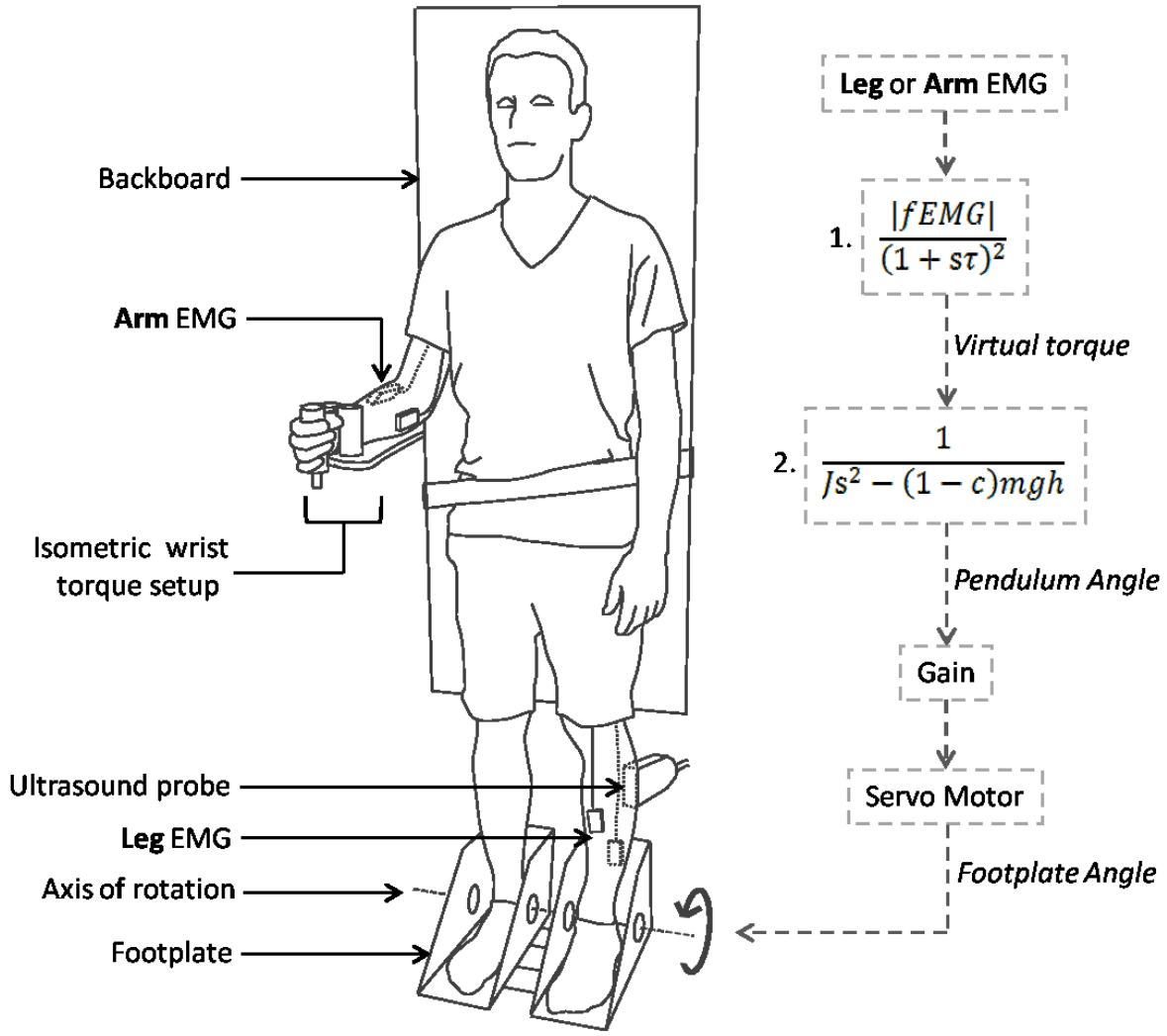

Figure 1. Experimental setup.

The subject balances a computer simulation of an inverted pendulum in real-time using only proprioceptive feedback. Using equation 1, a 'virtual torque' signal is constructed from flexor and extensor EMG of either the leg or the arm (depending on the experimental condition). The virtual torque acts on the model of the inverted pendulum shown in equation 2. The output of the model is the angle of the inverted pendulum. This is fed to a servo-motor via a gain block to determine instantaneous footplate angle. The footplates rotate around the axis of the ankle joints. The subject's body is immobilised against a static backboard such that all sensory feedback is provided through ankle rotation.

Experimental setup

The setup was designed so that the standing subjects' ankles could be rotated into dorsi-flexion and plantar-flexion while the rest of their body was immobilised against a static vertical backboard (Fig 1.) Subjects' feet were placed on two custom built footplates such that the axis of rotation of the ankles matched that of the footplates. The subjects were held against a vertical backboard by a horizontal Velcro strap secured around the waist. A single servo motor controlled the angle of both footplates which were mechanically coupled to move as one. Footplate angle was measured with a Hall effect precision potentiometer (CP 2UTX, Midori Precision Ltd, Japan). Ankle torque was recorded from each leg by two horizontally mounted load cells (Sensotec model 31, Sensotec Inc., USA. Not shown in figure – see Fig. 1A in chapter 3 for load cell diagram). Surface EMG (Delsys Bagnoli system) was recorded from the tibialis anterior and soleus muscles of the left leg. In addition, an ultrasound probe (5-10 MHz, DIASUS) was secured with a bandage to the medial gastrocnemius of the left leg, in a vertical plane perpendicular to the skin. This provided a view of both medial gastrocnemius and soleus muscles. The ultrasound machine was limited to a maximum of 40 seconds of recording. Thus, during each 120 second trial, ultrasound was automatically triggered to record from 70 - 110 seconds.

Firmly attached to the vertical backboard was a device that enabled recording of isometric wrist torque from the right arm. The subject rested their forearm on a horizontal metal platform, and grasped a solid round handle with their right hand. The hand was held passively in this position by bandaging the hand to the handle (not shown in diagram). The distal part of the forearm was prevented from moving by two adjacent foam supports so that a stiff strain gauge transducer attached to the handle could measure torques produced

by attempted flexion and extension of the wrist. Surface EMG (Delsys Bagnoli system) was recorded from the flexors and extensors of the wrist.

Experimental protocol

Upon presenting to the lab, every subject was able to familiarise themselves with all the equipment and procedures of the experiment. With eyes closed subjects balanced a virtual inverted pendulum using either their arm of leg muscles. The experiment was conducted in real-time at a sample rate of 1000 Hz (Simulink, Real Time Toolbox). The load was balanced using a myoelectric virtual torque signal constructed in real-time from surface EMG recordings either from the leg or from the arm. Raw EMG was high-pass filtered (60 Hz cut off), rectified, and then low pass filtered (Fig 1 – equation 1, where *fEMG* is high pass filtered EMG, *s* is the laplace variable, and τ is the time constant). This procedure transforms a raw EMG signal (which is noisy and contains a large bandwidth of frequencies) into a lower frequency smoothed signal that resembles a mechanical torque signal. The gain of the virtual torque signal was determined by linear regression with a mechanical isometric torque signal. The virtual torque signal acted on the virtual inverted pendulum to produce pendulum angle (Fig 1 – equation 2, where *J* = moment of inertia, *c* = proportion of torque provided by passive ankle stiffness, and *mgh* = total load stiffness). *J* is given by kmh^2 where *k* is a shape factor of 1.3 (Morasso & Schieppati, 1999), *m* is the subject's body mass, *h* is estimated from each subject's height, and *c* was set to 0.85 (Loram *et al.*, 2007*b*). Therefore, each load approximated each individual's 'human inverted pendulum'. Between trials, the gain between the sway of the virtual inverted pendulum and the angle of the footplates (the proprioceptive gain) was varied. For 'physiological' gain (gain = 1), as the load swayed forward by 1 degree, the subjects ankles were dorsi-flexed by 1 degree. When gain was

Control with Leg		**Control with Arm**	
Gain	Vision	Gain	Vision
0.33	No	0.33	No
0.5	No	0.5	No
1	No	1	No
2	No	2	No
3	No	3	No
0	Yes	0	Yes

Table 1. Summary of experimental conditions

equal to 3, as the load swayed forward by 1 degree the subjects' ankles were dorsi-flexed by 3 degrees. Thus, knowledge of the load angle was provided only through rotation of the ankles, and the ratio of pendulum angle to footplate angle (the proprioceptive gain) was varied among trials. Additionally, in two conditions the footplates did not rotate (gain = 0) and instead knowledge of load position was provided visually via the vertical position of a red circle displayed on a computer monitor. For six trials, subjects balanced the load using a virtual torque signal constructed from muscles of the lower leg (soleus and tibialis anterior). For a further six trials subjects balanced the load with the same method but using the flexors and extensors of the forearm. Details of each of the 12 conditions are shown in table 1.

Each formal trial was preceded by a practice trial where subjects could familiarise themselves with the particular proprioceptive gain setting. Subjects were informed that their primary aim should be to prevent the load from ‘falling over’, and that their secondary aim was to minimise sway. They were not required to keep the inverted pendulum at a specific angle. At the start of each trial, subjects were presented with a visual representation of the load on a computer screen in front of them. The angle of the virtual inverted pendulum was represented by the vertical position of a red circle on a black background. A small white cross marked the centre of the screen. Once each trial began, subjects were permitted to use vision to assist in balancing the load for a maximum of 20 seconds after which time they were instructed to close their eyes. If satisfactory control of the load could not be achieved in this time, the trial was aborted. The first 20 seconds of each successful trial was ignored in subsequent analysis. Four subjects began by completing all trials balancing with the legs before completing all trials balancing with the arm, and two

subjects completed trials balancing with the arm first followed by all trials balancing with the leg. Different gains were presented to subjects in a counterbalanced order.

Data analysis

All data were analysed using MATLAB 2011b (Mathworks). In each trial mean sway size was calculated by first determining the size of each individual unidirectional sway, and then averaging all individual sways together. To calculate the size of each sway, we identified the size of movements between inflection points in the sway record. We used the same procedure to determine the mean muscle movement size in each muscle length record. To calculate sway duration, we measured the time between each inflection point in the sway record and averaged this.

Automatic tracking of dynamic ultrasound videos

The ultrasound videos were analysed using commercially available tracking software (*Mocha for After Effects Leamington Spa, CV32 4TW, UK 2.6 – Imagineer Systems*). The principles of this technique have been described previously (Osborne & Lakie, 2011)**.** On the first frame of each ultrasound video, a spline was manually drawn around the edge of both soleus and medial gastrocnemius to determine the search area used by the tracking algorithm. The video was then automatically tracked. Once tracking was complete, further automatic refinements were made to compensate for any visible low frequency drift. Tracking data was then imported into a custom written MATLAB script which decoded each file and outputted muscle length change for each muscle in units of millimetres.

Simulations

In addition to the experimental work we wanted to use a simple model to explore the differences between balancing using the arm, where only voluntary control is permitted, and with the leg, where both voluntary and reflex control are possible. A schematic of the model is shown in Figure 2. We begin by describing our model of the condition where subjects balanced using the muscles of the arm.

Arm Simulations

The model consists of two basic elements: the unstable load and the controller. To model the load, we used the same six inverted pendula drawn from each of the experimental subject's body characteristics. To model the controller, we drew on work by Peterka (2000). Here, the author used a simple PID feedback controller to create realistic sway behaviour of an inverted pendulum. The PID controller consists of proportional (K_p), integral (K_I), and derivative (K_d) feedback gains. As in Peterka (2000), we set the parameters to K_p = 19.5 Nm/deg, K_I = 0.25 Nm/s/deg, and K_d = 4.5 Nms/deg. We selected a time delay based on recent work by Gawthrop *et al* (2009). The authors fitted both predictive and non-predictive feedback time delayed models to experimental data (human balancing of an inverted pendulum using a joystick). They found that, on average, the predictive model estimated a time delay of 211 ms, and the non predictive model estimated a time delay of 145 ms. The authors concluded that the predictive model estimated a considerably more realistic and physiologically appropriate time delay (Loram *et al.*, 2009*a*) than the non-predictive model. We agree with these conclusions. However, for simplicity, we omitted the predictive element from our model and used the time delay (145 ms) that produces similar performance to that of the predictive model. Thus, our model is not a realistic physiological representation, but a simplification that produces similar performance to a more complex,

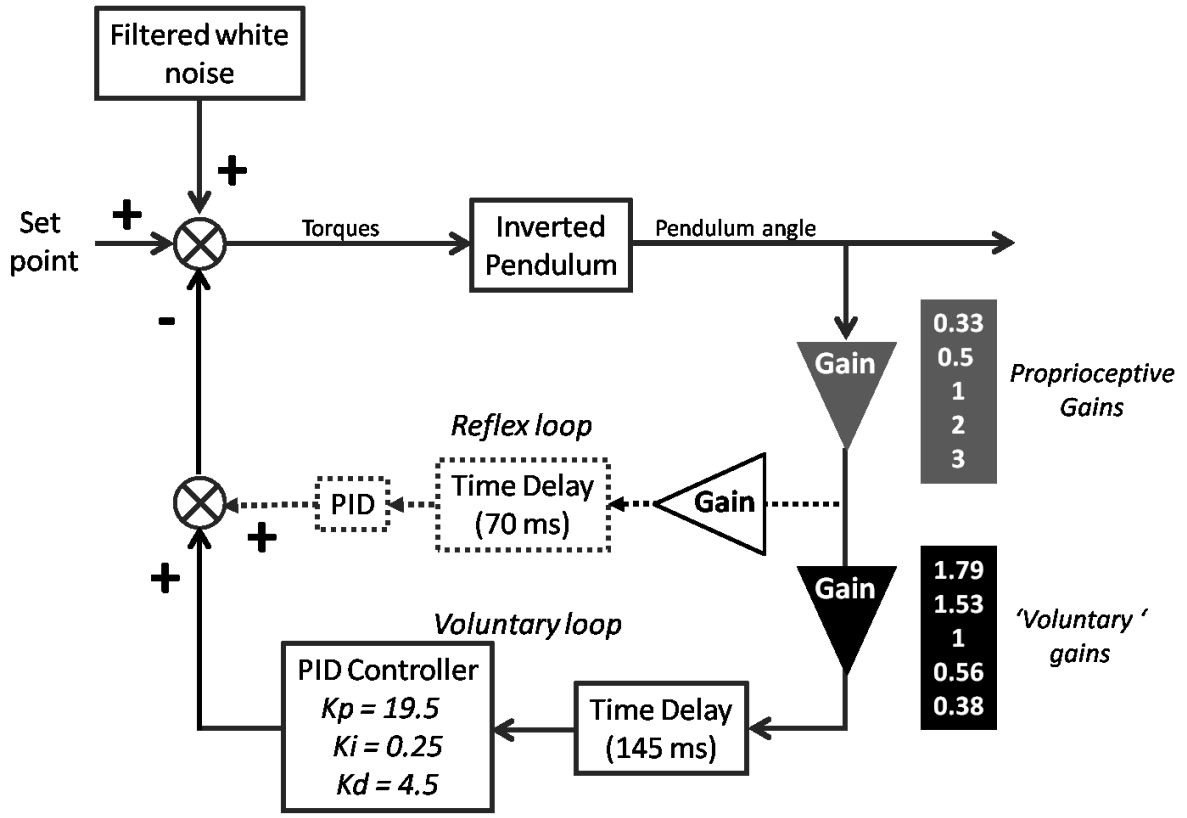

Figure 2. Simulations of arm control and leg control experimental conditions

In the model, an inverted pendulum is balanced by a simple PID feedback controller. The outer voluntary loop (solid black line) in isolation represents the arm control condition where only voluntary control is possible. The combination of both the outer voluntary loop and inner reflex loop (dashed black line) represent the leg control condition where both voluntary and reflex control are possible. The experimental manipulation of changing the proprioceptive gain is modelled by adding a gain block in the feedback loop (grey gain block). Voluntary modulation of feedback gain is also modelled through the voluntary gain block (black gain block). When modelling balance as a PID feedback controller, it is necessary to inject filtered white noise into the the system to produce realistic sway patterns.

but more realistic model equivalent. Finally, as with Peterka (2000)**,** low pass filtered Gaussian noise is summed with the control signal to produce realistic sway patterns.

In the present study we altered the 'proprioceptive' gain in different experimental conditions. To model this, we inserted a gain block in the feedback loop and altered the value to match the different experimental conditions (i.e. 0.33, 0.5, 1 etc). Comparing initial simulations with our experimental data quickly suggested that these feedback gains are also subject to voluntary modulation. We therefore inserted an additional gain block downstream which we considered to be a 'voluntary' gain to mimic the fact that subjects could alter their own feedback gain. This reflects the fact that subjects are not constrained to producing a torque response that is proportionally fixed to the size of ankle rotations, but can instead alter the size of their responses at will. We suggest that subjects learn the (average) size of torque response per unit ankle rotation that is suitable for each proprioceptive gain condition. Appropriate voluntary gains were calculated using a simple input output curve where the input was feedback gain and the output was mean sway size. This predictable relationship between total feedback gain and sway size enabled us to estimate the level of voluntary gain modulation based on the mean sway size in each experimental condition.

Leg Simulations

To simulate balancing with the legs we introduced the possibility of reflex control (Figure 2 – dashed line). In model terms, this simply consists of an additional feedback loop that is 'upstream' of the voluntary gain block (Figure 2 – dashed line). This means that the gain of this loop is always proportional to the gain in the particular experimental condition and is not influenced by any voluntary changes in gain. We selected a time delay of 70 ms to

reflect a 'lumped' reflex delay approximating both short and long latency reflexes (Diener *et al.*, 1984). However, we found that the time delay of this loop was not crucial: systematically changing this delay between 40 and 120 ms made no statistical difference to sway size in each of the experimental conditions.

Clarification of terms

Arm control condition/ Leg control condition. As described above we studied two experimental conditions: 'Arm control' - where subjects balanced the virtual inverted pendulum using the muscles of their forearm, and 'Leg control' – where subjects balanced the virtual inverted pendulum using their lower leg muscles. We refer to these two different experimental conditions as either the arm control condition or the leg control condition. We never use the word 'control' in the context of a 'control experiment' or 'scientific control'. Thus when we say 'leg control condition' we do not mean the 'control experiment' within the leg condition, we simply mean the condition in which subjects balanced the inverted pendulum using their leg.

Results

Experimental Results

Figure 3 shows representative traces from one subject. A 20 s snapshot of three trials of different gains are shown. In all cases the subject was balancing the load using their leg. In the first column (A,D, G), the proprioceptive gain was 0.33, in the second, 1, and in the third, 3. All panels in the top row (A - C) show both virtual inverted pendulum angle (light grey trace) and footplate angle (dark grey trace). The panels in the middle row (D – F) show the accompanying virtual torque signals constructed from soleus and tibialis anterior EMG. The panels in the bottom row (G - I) show change in muscle length of both medial gastrocnemius

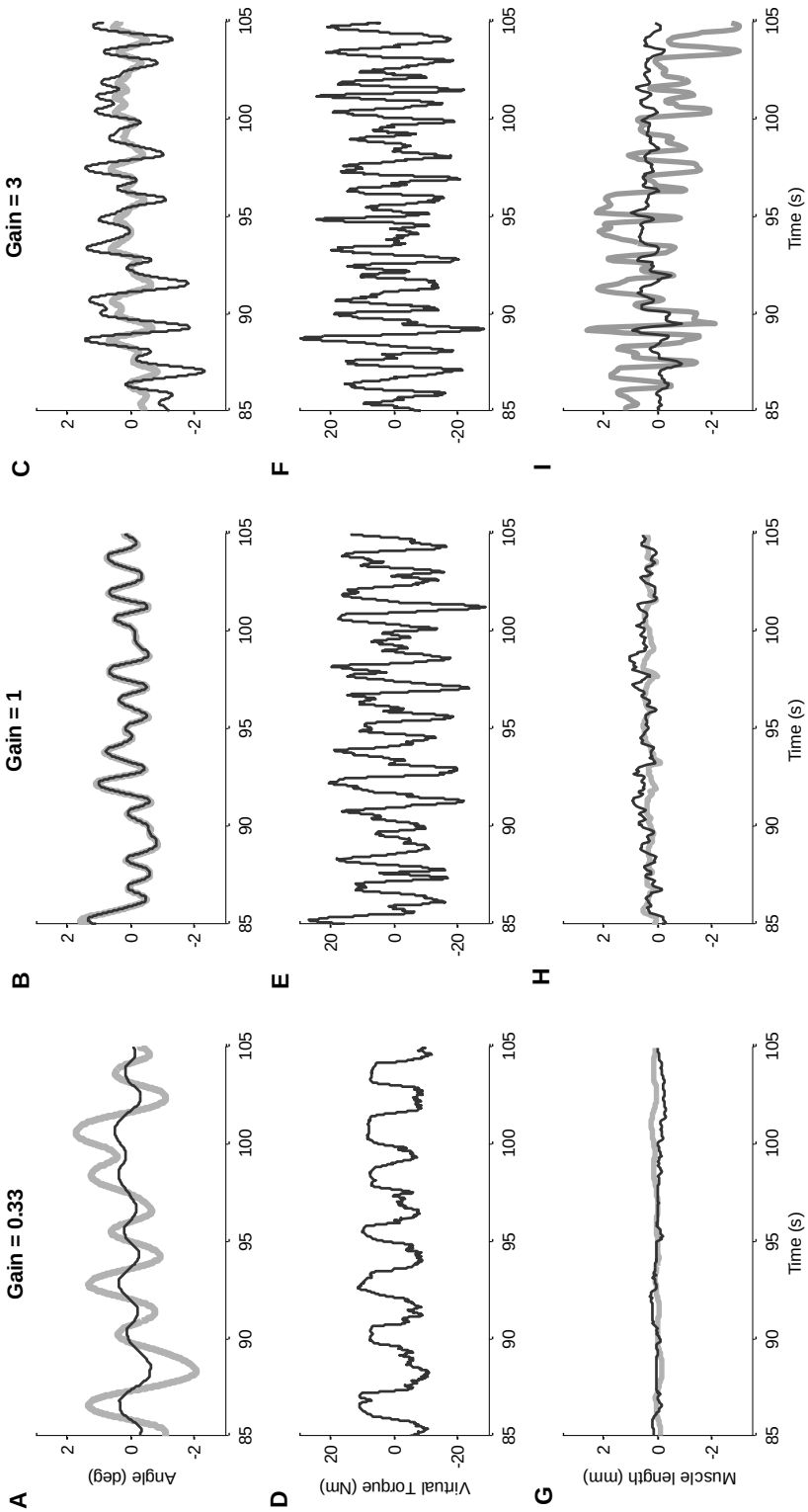

Figure 3. Representative trace. Details on next page.

Each column shows 20 seconds of data from a different trial. The title above each column denotes the proprioceptive gain setting in each trial. The top row (A-C) shows inverted pendulum ankle (light grey line) and footplate angle (black line). The instantaneous footplate angle is the product of the instantaneous inverted pendulum angle and the particular proprioceptive gain setting in any given trial. The middle row (D-F) shows the corresponding virtual torque signals. The bottom row (G-I) shows the corresponding change in muscle length for both medial gastrocnemius (light grey line) and soleus muscles (dark line).

(light grey trace) and soleus muscles (dark trace). The effect of changing the proprioceptive gain is visible even in these short sections of data.

In general, the average sway size of the pendulum tended to decrease as the proprioceptive gain increased. Concomitantly, the interval between sways tended to decrease. The average sway size of the footplate tended to increase as the proprioceptive gain increased. The virtual torque traces grew slightly larger with increased gain. This was accompanied with more prominent high frequency torque fluctuations. The change in length of both soleus and gastrocnemius muscles dramatically increased with higher gains.

Figure 4 summarises the key findings from the experimental data from all subjects. Data from the 'arm control condition' are presented in the left column (A-D), and data from the 'leg control condition' are presented in the right column (E-H). The top row (A and E) shows the mean sway size of the pendulum (light grey line) and the mean sway size of the footplate (dark grey line) for the different proprioceptive gain settings. A two-way ANOVA revealed significant main effects of both mode of control ($p < 0.001$) (either using the arm or legs) and proprioceptive gain ($p < 0.001$) on load sway size. No significant interaction was found. Statistical analysis on the footplate data revealed the same main effects and no interaction. The main effect of mode of control showed that average sway size (both load and footplate) was significantly larger when controlling with the arms than with the legs (compare 4A with 4E). The main effect of proprioceptive gain is clear from visual inspection: inverted pendulum sway size systematically decreased as proprioceptive gain increased and footplate movement size concomitantly increased (Fig 4A and 4E light grey trace). We are more interested in this general effect than the precise statistical difference between conditions so we did not consider post hoc pair wise comparisons. We found no statistical

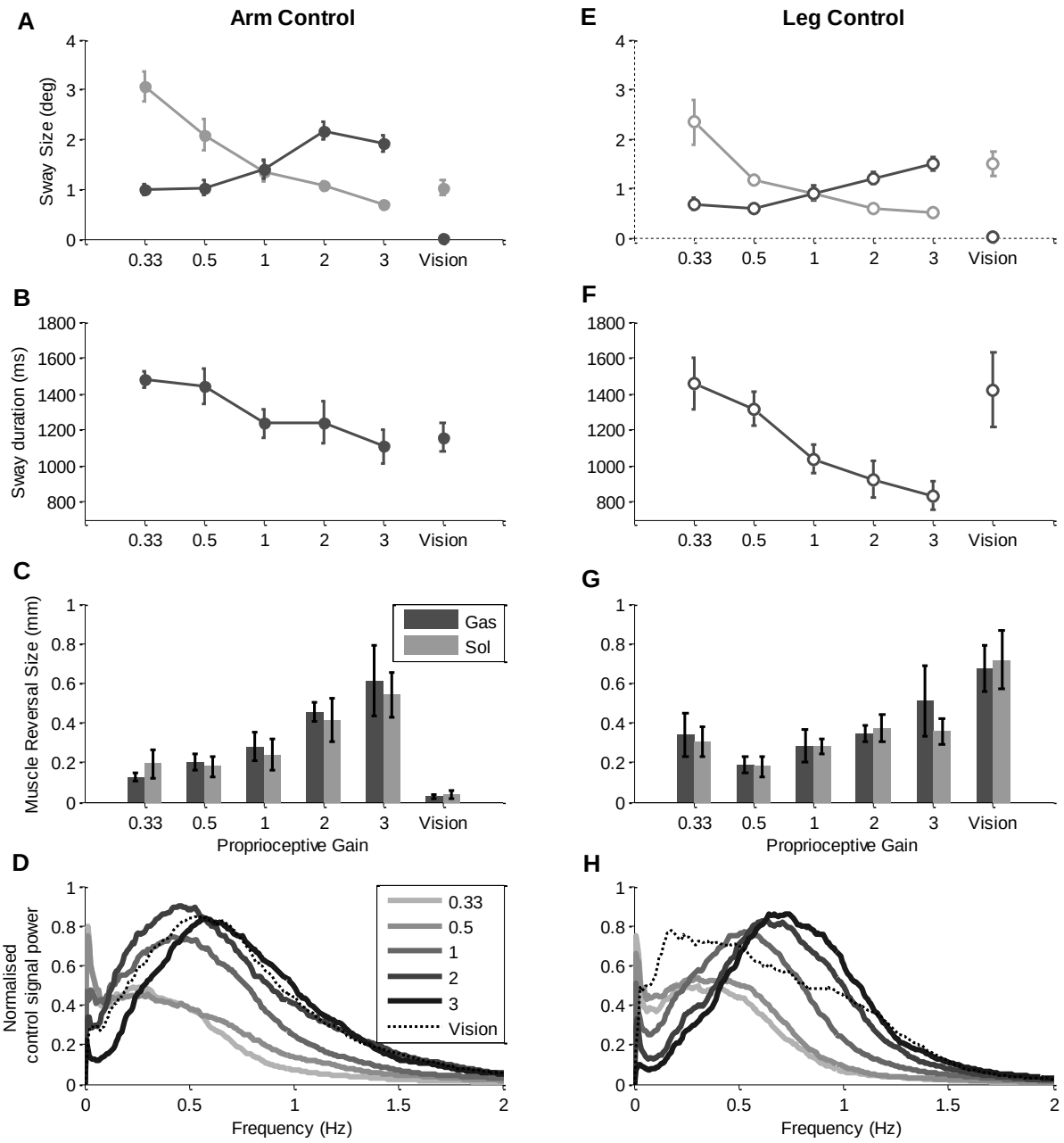

Figure 4. Grand average results.

The left-hand column (A – D) shows the results from the arm control condition and the right-hand column (E – H) shows the results from the leg control condition. The top row (A and E) show the mean sway size of the inverted pendulum (light grey trace) and the mean size of footplate movements (dark grey trace) in the different proprioceptive gain conditions and in the vision only condition. The second row (B and F) shows the mean sway interval. The third row (C and G) shows the mean muscle movement size (size between position reversals) for both medial gastrocnemius (Gas) and soleus (Sol) muscles. The bottom row (D and H) shows the normalised amplitude spectra of the control signal (the virtual torque signal). All plots show mean ± SE.

difference in performance between controlling with the arm or leg when using only visual feedback (Fig 4A and 4E light grey circles in vision condition, paired samples t-test).

The second row from top (B and F) shows the mean interval between sways (sway duration) over the different proprioceptive gain settings. A two-way ANOVA revealed significant main effects for both mode of control ($p < 0.005$) and proprioceptive gain ($p < 0.001$) on sway interval. We did not find a significant interaction. Mean sway interval was significantly longer in the arm control condition (Fig 4B) than in the leg control condition (Fig 4F). We note that in the data this difference appears more pronounced at higher gains. Once more, visual inspection of the data shows that sway duration systematically decreases as a function of proprioceptive gain so we did not consider post hoc pair wise comparisons. The third row from top (C and G) shows the mean size of muscle movements of both medial gastrocnemius and soleus muscles. A two-way ANOVA revealed significant main effects for proprioceptive gain on both soleus ($p = 0.05$) and gastrocnemius ($p = 0.01$) movement size. We found no significant interaction effect and no main effect for mode of control. Post hoc pair-wise comparisons revealed that gastrocnemius muscle movements were significantly larger at the highest proprioceptive gain setting than the two lowest proprioceptive gain settings. Soleus muscle movements were found to be significantly larger at the highest proprioceptive gain settings than at a proprioceptive gain of 0.5.

We note that at the lowest proprioceptive gain setting (0.33) the average muscle movement size appears to be larger when controlling with the leg (Fig 4 G) than the arm (Fig 4C) but this observation is not justified statistically. Finally, the bottom row (D and H) show normalised power spectra of the virtual torque signal for all proprioceptive gains. Table 1 shows the average peak frequency in each condition. In general, the peak frequency was

higher in the leg control condition than the arm control condition. In both leg and arm control conditions, control was dominated by very low frequencies when proprioceptive gain was below 1. When proprioceptive gain was greater than or equal to 1, the virtual torque signal was dominated by higher frequencies. This effect appears most pronounced in the leg control condition.

As mentioned above we observed superior performance (smaller sway size) in the leg control condition compared with the arm control condition. To remove any fundamental difference in task difficulty and provide a more direct comparison of the effect of gain change in each task, we normalised each data set relative to the physiological gain setting (gain = 1). Figure 5A shows the relative sway size of the virtual inverted pendulum in both the arm control condition (filled grey circles) and the leg control condition (white circles). The corresponding observations of footplate movement are shown in Figure 5C. The difference in relative sway size between leg control and arm control is more apparent in the footplate movement than the pendulum sway. This is because, at high gains, even small differences in pendulum sway size translate to large differences in footplate movements. Statistical analysis (two-way ANOVA) revealed a significant interaction ($p < 0.001$) between mode of control and proprioceptive gain on footplate movement size. Post hoc pair-wise comparisons showed that mean platform movement was significantly greater when controlling with the arm at a gain of 2 ($p < 0.01$). Arm control also appeared inferior at a gain of 3 but this difference was not statistically different ($p = 0.16$). Perhaps more striking than the statistics is a visual inspection of the data. At low gains, the two conditions (arm control and leg control) are indistinguishable, but at gains greater than 1 there appears to be a clear difference.

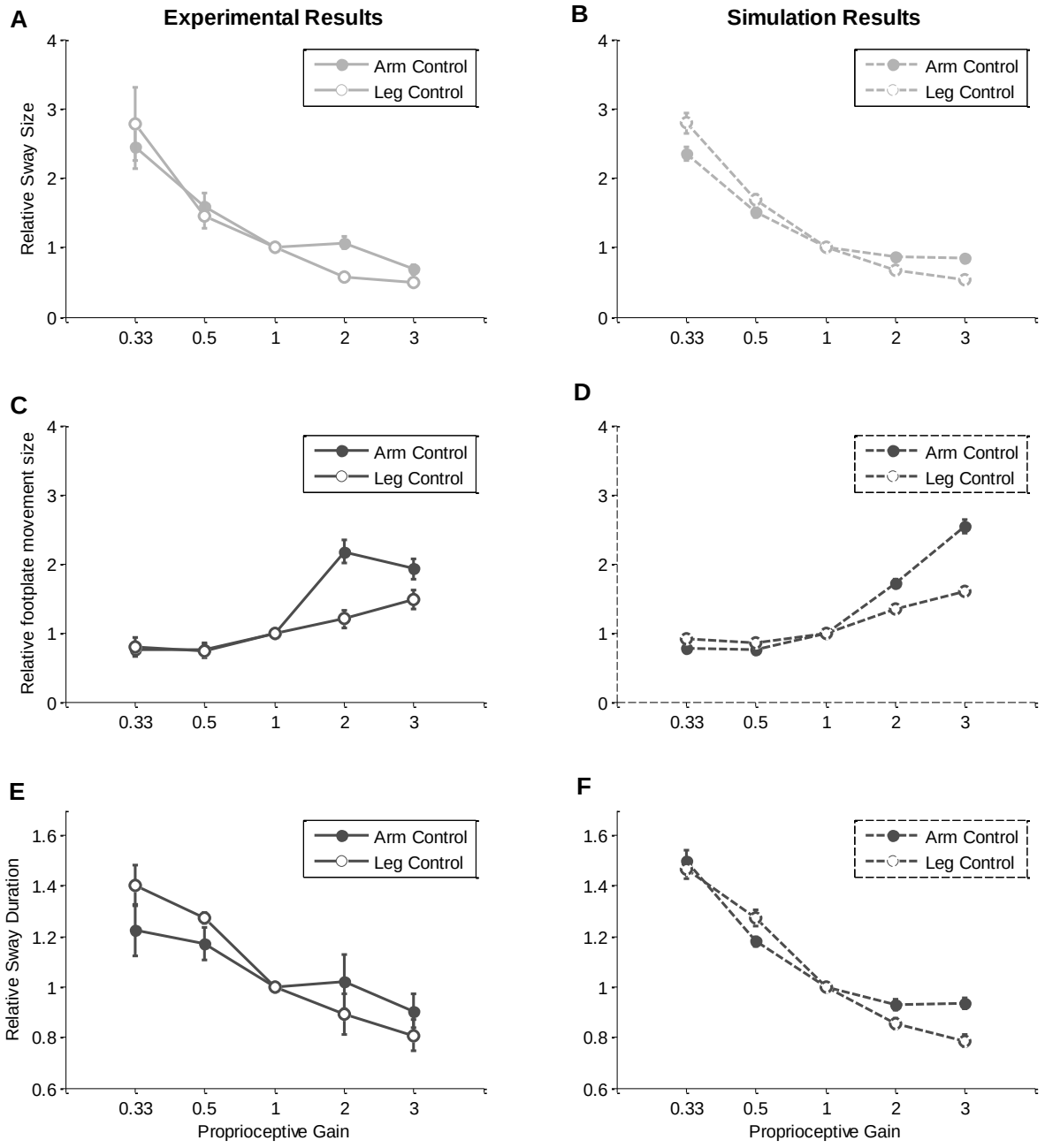

Figure 5. Comparison of experimental and simulation results.

The first column (A, C, E)shows the experimental results of both leg control and arm control normalised to the physiological proprioceptive gain condition (gain = 1). This allows for a more direct comparison of performance between arm and leg control. The second column (B, D, F) shows the normalised data from the simulations. The top row (A and B) show relative sway size. The second row (C and D) show relative footplate movement size. The bottom row (E and F) shows relative sway duration. All plots show mean ± SE.

	0.33	**0.5**	**1**	**2**	**3**	**Vision**
Arm control Peak frequency (Hz)	0.097 ± 0.17	0.122 ± 0.24	0.300 ± 0.23	0.417 ± 0.17	0.519 ± 0.25	0.451 ± 0.22
Leg control Peak frequency (Hz)	0.131 ± 0.19	0.139 ± 0.20	0.382 ± 0.27	0.565 ± 0.27	0.715 ± 0.17	0.380 ± 0.24

Table 2. Peak frequency of control signal (virtual torque) in each experimental condition. Numbers are mean ± SE.

Figure 5E shows relative sway duration (again normalised to gain = 1 setting) in both the arm control condition (filled grey circles) and the leg control condition (white circles). A two-way ANOVA revealed significant main effects for gain ($p < 0.001$) but not for mode of control. We found no significant interaction. However, we note that at gains lower than 1, the relative sway duration is higher when controlling with the leg whereas at gains higher than 1, the relative sway duration is lower. Thus, the effect of gain on relative sway duration appears more pronounced when controlling with the legs than with the arms.

Simulation Results

The corresponding results from the simulations are plotted in Figure 5B, D and F. Again, the arm condition is shown by the filled grey circles and the leg condition is shown by the white circles. The model reproduces the key features we observed in the experimental data. Relative sway size is statistically indistinguishable when gain is less than 1, but is significantly smaller in the leg control condition when gain is greater than 1 (Fig 5B and D). Again this effect is most obvious when looking at the footplate data (Fig 5D). Additionally, the effect of gain on sway duration is slightly more pronounced when controlling with the legs when compared to the arm condition (Fig 5F) which broadly matches the experimental data (Fig 5E).

Discussion

In the present experiments we used a novel paradigm to enable a comparison between *reflex + higher level control* and *higher level control only.* We asked subjects to balance an inverted pendulum using either the muscles of the leg (leg control) or the muscles of the forearm (arm control). This allowed us to compare two conditions: one where reflex and

higher level control were possible (leg control), and one where only higher level control was possible (arm control). Further to this we studied the effect of altering the proprioceptive gain on task performance. This was made possible by replacing the real inverted pendulum with a computer model of an inverted pendulum (the virtual inverted pendulum). The computer model outputs the angle of the pendulum in real-time which is used to drive a servo-motor to control the angle of the footplates. This enables us to change the gain between the virtual inverted pendulum output and the footplate angle and therefore alter the 'proprioceptive gain'. To balance the virtual inverted pendulum we used a virtual torque signal constructed from EMG instead of a real measurement of torque. This was important in the leg control condition because real ankle torque is composed of both active and passive components. The passive torque component, at least for small sways, is proportional to the size of ankle rotations (Loram *et al.*, 2007*a*). The means that if proprioceptive gain is above 1, the passive resistance to ankle rotation is artificially high, and if proprioceptive gain is below 1, the passive resistance is artificially small. To avoid this confound we created a virtual torque signal from EMG to exclude all passive torque components.

Our investigations centred on how altering proprioceptive gain affected task performance. Subjects were instructed to try and minimise sway where possible but were not instructed to balance the inverted pendulum at a specific angle. This allowed the task to take on a more natural feel akin to quiet standing where large low frequency fluctuations in position are common (Peterka, 2000). We therefore elected to use mean sway size as a measure of performance. Mean sway size in each trial is calculated from each individual unidirectional sway (Loram *et al.*, 2005*c*) over a 100 second period. This eliminates low frequency

components of sway but still provides a measure of how well the inverted pendulum is under control.

Experimental data

Figure 4A shows the mean sway size of the inverted pendulum (light grey trace) and of the footplate (dark grey trace) at different levels of proprioceptive gain in the arm control condition. The corresponding data for the leg control condition are shown in Figure 4E. The sway size of the inverted pendulum and the movement of the footplates are related. This is because the angle of the footplates was determined in real-time by the product of the proprioceptive gain setting and the instantaneous virtual inverted pendulum angle. Thus, an inverted pendulum sway of 1 degree at a proprioceptive gain setting of 3 would have resulted in a footplate movement of 3 degrees (1 x 3). In both arm and leg control conditions it is clear that increased proprioceptive gain reduced the mean sway size of the inverted pendulum. This might be expected. When proprioceptive gain is very low (e.g. 0.33) even moderately sized sways will only be converted into small ankle rotations. It is known that perceptual thresholds of ankle rotation during standing are in the order of one tenth of a degree (Fitzpatrick & McCloskey, 1994). By this logic, when the gain is set to 0.33, inverted pendulum sways less than one third of a degree will remain undetectable. By contrast, the inverted pendulum need only sway three to four hundredths of a degree before becoming consciously perceptible in the highest gain condition (gain = 3).

It is interesting that the footplate movement size actually increased with higher proprioceptive gain. This probably reflects the difficulty of exerting a very fine level control. When proprioceptive gain is high (e.g. 2 or 3) small sways of the pendulum translate into large footplate excursions. The temptation of a naive subject is to respond with an excessive

corrective force that is proportional to the size of the ankle rotation. Large corrections (high gain responses) in time delayed systems lead to instability. Indeed, subjects almost always lost control of the inverted pendulum due to overzealous efforts. To master the high proprioceptive gain conditions, subjects must learn to exert corrective responses that are small in proportion to the size of the ankle rotations. It is likely that there is a limit to the level of fine control that is sustainable. The result is that footplate movements in the high gain conditions are larger.

With the exception of the vision only conditions, balancing with the leg was a superior method to balancing with the arm (Fig 4A vs 4E). This difference may be explained by the disparity in familiarity between the two tasks. Balancing an inverted pendulum with the ankle musculature has many similarities to balance during normal quiet standing (Fitzpatrick & Taylor, 1992; Fitzpatrick *et al.*, 1992, 1994*b*; Loram *et al.*, 2001; Loram & Lakie, 2002*a*). Previous experiments have shown this task is possible even when sensory inputs are limited to lower leg muscle afferents (Fitzpatrick *et al.*, 1994*b*). This is different from balancing the inverted pendulum using forearm muscles. Hand balancing of an inverted pendulum in the context of visuo-manual control has been studied quite extensively. This is normally accomplished through a joystick (Loram *et al.*, 2009*a*, 2010) or via a mechanical linkage (Lakie *et al.*, 2003; Loram *et al.*, 2006*a*). Even naive subjects become quite proficient at this sort of visuo-manual control. Indeed, in the current experiments subjects could easily balance the inverted pendulum using the arm when presented with visual feedback (Fig 4A vision condition). However, hand balancing using only proprioceptive feedback from the lower legs is a very novel task. While all subjects had considerable practice and were

competent in both arm and leg control prior to any data collection, the results suggest that they remained slightly more proficient when controlling with the leg.

We are most interested in how changes in proprioceptive gain affected performance irrespective of absolute task difficulty. Consequently, we normalised mean sway size against the physiological proprioceptive gain condition (gain = 1). This allows us to view the relative impact of changes in sensory gains and permits a more direct comparison of the leg control and arm control conditions. The results of these data are shown in Figure 5. In Figure 5A, the relative sway size of the inverted pendulum is plotted for both arm control (filled grey circles) and leg control (white circles). Figure 5C shows the relative size of footplate movements for both arm control (filled grey circles) and leg control (white circles). At low gains (gain < 1) there is no distinguishable difference between arm control and leg control. However, Figure 5C in particular suggests that at high levels of proprioceptive gain (gain > 1) leg control performance (dark grey circles) was superior to arm control performance (white circles). This was confirmed statistically by a significant interaction of mode of control (arm or leg control) and proprioceptive gain on footplate movement size. Thus, at low gains relative performance is identical regardless of the modes of control, but at high gains leg control is superior.

Why is leg control proportionately superior at higher gains? We cannot provide a conclusive answer to this question with the methods employed in the current experiment. However, both experimental observations and simulation results are consistent with this difference being explained by reflex control. This proposition requires a number of assumptions, and further experiments are required to validate our hypothesis, but the explanation is attractive in its simplicity and highly plausible biologically.

There are two major differences between the leg control and the arm control conditions. The first is task familiarity, and the second is the availability of reflexes. We contend that we have removed the effect of task familiarity on performance by normalising the data to the physiological gain condition. We see no reason why task novelty should mean arm control is proportionately more difficult than leg control at high gains. This leaves the second major difference between the two modes of control: the availability of reflexes. When controlling with the arm and 'listening' with the feet, the subject is engaging in an entirely voluntary manual control task. We do not know of any mechanism whereby additional stability can be provided through reflex pathways in such a complex task. In contrast, the reflex pathways available in the leg control condition are well described. Broadly speaking such responses may be categorised into short loop reflexes that do not transcend the spinal cord (≈ 50 to 60 ms) or long loop reflexes that may travel via the brainstem and/or cerebellum (≈ 100 to 150 ms) (Nashner, 1976; Diener *et al.*, 1984; Loram & Lakie, 2002*b*). It has previously been shown that these responses tend to resist changes in ankle angle, which under conditions of support surface tilt, can be destabilising (Nashner, 1976; Loram & Lakie, 2002*b*). However, in the current experiments where the subject is splinted so that the body cannot move, any resistance to change in ankle angle will be facilitative and help stabilise the inverted pendulum. Thus, in the leg control condition, in addition to voluntary pathways, reflex pathways are available and, if present, should serve to improve performance.

Relative performance using leg control is only superior at high proprioceptive gains. Why would reflexes confer an advantage at high but not low proprioceptive gains? In the higher gain conditions the average size of ankle movements is larger than in the low gain conditions (Fig 4A and E – dark trace shows ankle movement sizes). Additionally, sway

duration is shorter in high gain conditions (particularly in the leg control condition – compare Fig 4B with 4F) meaning the average speed of sways also increases with higher proprioceptive gains. Concomitantly, calf muscle movements, which potentially are a major source of proprioceptive information (Fitzpatrick & McCloskey, 1994; Fitzpatrick *et al.*, 1994*b*) also increase in size (Fig 4C and G). These effects are also visible in an individual trace (Fig 3). Previous experiments have found that the amplitude of reflex responses are proportional to the size, and to a lesser extent the speed of ankle perturbations during standing (Diener *et al.*, 1984). Thus we might expect the role of reflexes to be more prominent in the higher gain conditions. There is conflicting evidence as to whether reflex gain can be modulated voluntarily (Nashner, 1976; Ludvig *et al.*, 2007; Manning *et al.*, 2012). In the present experiments the addition of reflex control will always confer an advantage. This is because reflex control, at its most simple, operates as a negative feedback servo system that will attempt to maintain ankle angle. In these experiments, where sways are reflected by changes in ankle angle, such a system would provide useful corrective responses to dampen sways. Additionally, the shorter time delay of the reflex pathways will enable higher gain responses without threatening the stability of the system. Consequently, we suggest that any reflex involvement should facilitate balance and we would not expect any significant attenuation of these stabilising responses.

Other data from the experiment are consistent with the hypothesis that reflexes contribute to enhanced performance in the leg control condition. Figure 4D and H show normalised power spectra of the virtual torque signal for each experimental condition. The progression from the lowest gain to the highest is denoted by the intensity of the line colour (the lowest gain is the lightest shade and the highest gain is the darkest shade). When the

proprioceptive gain is less than unity the spectra are very similar in both arm control and leg control conditions. They are dominated by low frequencies in both cases. In the arm control condition (Fig 4D) when proprioceptive gain is higher than unity, the spectra shift to higher frequencies (around 0.3 – 0.5 Hz), and there is a small rise in peak frequency as gain increases (table 2). In the leg control condition, this relationship is more pronounced: there is a larger rise in peak frequency as gain increases (Fig 4H and table 2). The higher frequencies that we observe in the virtual torque signal of the leg control condition are consistent with increasing reflex contribution because reflex responses are associated with shorter delays and therefore higher bandwidth control. We must, however, be cautious in this interpretation. We are reporting descriptive measures from a closed loop system where it is impossible to disentangle cause and effect (Van der Kooij *et al.*, 2005; van der Kooij & van der Helm, 2005). We cannot establish whether higher frequency control (Fig 4H) causes shorter sway durations (Fig 4F), or whether shorter duration sways cause higher frequency control. We consider this evidence supportive but circumstantial.

Simulation data

Our experimental observations are consistent with a simple hypothesis that: 1) Reflex control is present when balancing with the legs, and 2) reflex control has a greater influence in the high gain conditions because of larger faster ankle rotations. We created two simple models (one of arm control and one of leg control) to try and capture the main features of our experimental results. The arm control model contains a 'voluntary control' feedback loop, and the leg control model contains both voluntary and reflex feedback loops.

A schematic of both models is shown in Figure 2. We began by modelling the simpler arm control condition. This consists of a single voluntary feedback loop with PID controller and

appropriate time delay (solid black line labelled voluntary loop). To mimic the experimental manipulation of changing the proprioceptive gain we inserted a gain block into the feedback loop (labelled Proprioceptive Gains). For fair comparison with our experimental data we used mean sway size over 100 seconds of simulation data as a measure of performance. Initial simulations with these parameters showed that the model could not recreate the experimental data. The lowest proprioceptive gain condition produced sways three times larger than the experimental data, and in the highest gain condition the model became completely unstable. We therefore reasoned that there can be some voluntary modulation of the proprioceptive gain: the corrective response need not bear an unchanging relationship to the sensory signal. This is physiologically plausible as we are modelling arm control where the subject can readily modulate the size of their corrective responses at will. Consequently, we introduced a further voluntary gain block (labelled voluntary gains) downstream of the proprioceptive gain block. Simple optimisation allowed us to calculate the magnitude of voluntary gain modulation in each proprioceptive gain condition in order to produce a sway size that corresponded well with our experimental results. The respective 'voluntary gains' are shown in Figure 2 (for example, when proprioceptive gain is set to 0.33, the subject partially compensates by increasing their voluntary gain to 1.79). As would be expected, this simple model reproduced the experimental results well.

To model the leg control condition we added a second 'reflex' feedback loop (Fig 2 – dashed line labelled reflex loop). In line with our expectation that the reflex contribution would, at least to an extent, depend on the size of the sensory signal (Diener *et al.*, 1984) we placed this loop upstream of the voluntary gain modulation block. This means that all contributions from this loop are proportional to ankle rotation. We added two additional parameters: 1)

an appropriate 'reflex' time delay, and 2) a single gain block. Systematic analysis showed that varying the time delay over a wide range (40 to 120 ms) made very little difference. We present results from a model with a time delay of 70 ms. We found that the gain block had a greater impact on the simulation results. We ran a simple optimisation procedure and found that a gain of 0.22 gave the best fit to the experimental results. This reflex gain is simply a constant. It remains the same regardless of experimental condition. In the feedback loop the reflex gain block (white gain block) is downstream of the proprioceptive gain block (light grey gain block). This means that the total reflex loop gain is the product of the proprioceptive gain (which changes) and the reflex gain (which does not change). Finally, for simplicity, we used the same PID controller in the reflex loop as we did in the voluntary loop. The results of all simulations are shown in the right hand column in Figure 5. These may be compared with the experimental results shown in the left hand column. Arm control is denoted by the traces with full grey circles and leg control is denoted by traces with white circles. The simulation reproduces the key features of the experimental results. Performance in the arm (filled grey circles) and leg control (white circles) conditions is indistinguishable at low gains. However, at gains greater than 1, leg control performance is superior (sway size – top row, and footplate movement – middle row, are smaller) because of the increasing contribution of the reflex loop. We also note that the simulation broadly reproduces the difference in relative sway intervals (Fig 5, bottom row). Changes in proprioceptive gain have a greater impact on sway interval in the leg control condition (white circles) than the arm control condition (filled grey circles).

What can we conclude about the relative contribution of both reflex and voluntary pathways towards balance control in this task? Our model optimisation found a reflex gain

of 0.22 gave the best fit to the experimental results. This means that under physiological proprioceptive gain conditions, where voluntary gain is 1 (see Figure 2), the reflex pathway constitutes 27 % of the total control output. However, in this artificial balancing task, ankle rotations (and sway sizes) are larger than during normal quiet standing (Loram *et al.*, 2005*c*), and as such we might expect the contribution in quiet standing to be smaller. However, it is very difficult to estimate the true contribution of reflex pathways even in this artificial task. These estimations are based on relative performance data where sway size has been normalised to the physiological gain condition (gain = 1). We normalised the data because performance using leg control was generally superior to performance using arm control. In normalising the data we are assuming that the voluntary pathways involved in arm and leg control are essentially identical but that leg control is simply more familiar, and that the residual difference in performance between tasks is a result of reflex involvement. While this is unlikely to be completely true, we suggest that the voluntary pathways are broadly the same because they are engaging in the same task and using the same sensory source: only the motor output is different. It is difficult to give an accurate estimate of the reflex contribution to balance control but our observations suggest that reflex control is present, and increases its contribution at higher gains where ankle movements are larger. The simulation results demonstrate that, given a low enough threshold, the presence of a reflex loop could be masked by a more dominant higher level loop if ankle rotations are small.

Conclusions

In conclusion, we have offered a simple and plausible explanation for our experimental results. Further direct physiological evidence would support or refute our hypothesis. The experiment could be repeated with the addition of a continuous unpredictable

perturbation. This would enable an estimate of the time delay between the perturbation and corrective responses (Van der Kooij *et al.*, 2005; Loram *et al.*, 2009*a*) allowing a greater insight into the pathways responsible for the control output. Perturbation studies may be criticised because they change the very nature of the task under investigation so a comparison with the conclusions of the present study would be highly informative. Crucially, we believe there is merit in allowing room for both reflex and higher level pathways in balance control investigations. Often experiments begin with a hypothesis that balance is controlled either by reflexes (Nashner, 1976; Fitzpatrick *et al.*, 1992, 1994*a*; Lockhart & Ting, 2007; Welch & Ting, 2008), or by higher level processes (Loram *et al.*, 2005*c*). The observations from the present experiment suggest that balance control may be best explained by allowing room for both.

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Chapter 5

SENSORY REDUNDANCY IN HUMAN VISUO-MANUAL INTERMITTENT CONTROL

ABSTRACT

Recent experiments have shown that performance in a manual joystick control task is slightly superior if subjects adopt an explicitly intermittent control strategy of tapping the joystick instead of holding it continuously. It has been suggested that control by gentle taps promotes higher quality sensory feedback than sustained control. We wished to test this hypothesis using a novel paradigm in a manual control task.

With ethical permission and their informed consent, subjects (n = 20) sat in a self selected position holding a small uni-axial joystick and wore a pair of PLATO visual occlusion spectacles. A computer screen in front of them displayed both a red circle, which represented the angle of a virtual inverted pendulum, and a white cross which marked the centre of the screen. Subjects were required to maintain the position of the circle as close to the centre of the screen as possible via gentle taps of the joystick. As subjects performed the task, their vision was occluded for a period of 200 ms following each contact with the joystick. In different trials, the delay between joystick contact and the 200 ms visual occlusion was varied among the following values: 1 ms, 50 ms, 100 ms, 150 ms, 200 ms, 250 ms and 2000 ms. There was also a control condition where no occlusions were presented throughout the whole trial.

In the control condition, and in the 2000 ms condition, the modal tapping intervals consistently occurred at around 390 ms. In the 1, 50, 100 and 150 ms conditions the modal

tapping intervals consistently occurred at a relatively fixed interval following the end of the occlusion (250 ms). In the 200 and 250 ms conditions, there were two common tapping intervals. The modal tapping intervals were 381 and 376 ms respectively, and there was a secondary peak at 258 and 257 ms following the end of the occlusion. Performance in the task appeared least impaired compared to the control condition when the occlusion was presented after only a 1 ms or 50 ms delay.

These observations suggest that, in this particular task, subjects were able to compute, select and execute a corrective response (a tap of the joystick) within ≈ 260 ms of the presentation of visual information. However, when subjects were not occluded, or when the delay between the tap and the occlusion was long (2000 ms), subjects elected to make corrective responses at longer intervals (approximately 390 ms). We suggest this discrepancy may be explained if each tap is immediately followed by a brief period of 'sensory redundancy' where subjects make little use of sensory information. This may also explain why performance was least impaired when the visual occlusion was presented immediately following each tap because in this case, the visual occlusion is partly concurrent with the self-occlusion. We present a conceptual model where control by tapping proceeds as alternating epochs of action and sensation.

Introduction

Control of standing balance in humans is an intriguing problem because of the precarious nature of bipedal stance. Upright man is tall and has a proportionately small base of support which means the centre of mass must be kept within a small range for balance to be maintained. There is still no consensus as to how this achieved. Some groups believe balance maintenance is solved automatically by lower level neural structures (Deliagina *et al.*, 2007; Lockhart & Ting, 2007; Welch & Ting, 2008). Others have found problems with this traditional paradigm (Loram *et al.*, 2004) and have pointed to remarkable similarities between human manual control and quiet standing control (Lakie *et al.*, 2003; Loram *et al.*, 2005*c*). The study of voluntary manual control has led to important insights that may apply to postural maintenance in general (Lakie *et al.*, 2003; Lakie & Loram, 2006; Loram *et al.*, 2006*a*, 2009*c*, 2010, 2012).

Prompted by the discovery that human ankle stiffness is below that required for passive stability (Loram & Lakie, 2002*b*; Casadio *et al.*, 2005; Loram *et al.*, 2007*b*), a group of authors posed a simple question: how is manual human balance of an unstable load achieved? Lakie *et al* (2003) asked subjects to balance an inverted pendulum, with similar dynamics to that of a standing human, through a compliant linkage. Subjects pulled on a handle that was attached to a spring which in turn was attached to the inverted pendulum. This paradigm requires that subjects make corrective actions to keep the load balanced. If the handle were held perfectly still, the load would fall over because the spring is too compliant to passively stabilise the load. The compliant linkage also means that the hand and the load are not constrained to move together – they are decoupled. Analysis showed that balance was accomplished through what looked like distinct pulsatile movements of the hand at a rate of

around two to three per second. This was considerably faster than the average unidirectional sway duration of the inverted pendulum (one second). In further experiments the stiffness of the spring connecting the hand to the inverted pendulum was varied. The sway size of the inverted pendulum and the size of hand movements increased systematically as a function of decreasing spring stiffness. However, the frequency of sway and frequency of hand adjustments was remarkably consistent regardless of the spring stiffness. Additional studies have shown the frequency of control adjustments in this task to be largely invariant in the face of changing load dynamics (Loram *et al.*, 2006*a*, 2009*a*, 2010), sensory modality, sensory abundance, and sensory gain (Lakie & Loram, 2006), and explicit control strategy (minimise position vs. minimise velocity) (Loram *et al.*, 2010). This strongly suggests that these experiments have revealed an intrinsic property of the human neural controller, at least with regard to the balance of second order loads.

It is known that, when pushed to oscillate a joystick as fast as possible, humans can do so at around 6 Hz, or twelve position reversals per second suggesting that the rate of outputs is not limited by the motor system (Loram *et al.*, 2006*a*). Why then, are corrective actions in a balancing task limited to two to three per second? Seminal experiments by Craik showed that unless there is a gap greater than half a second between two successive stimuli, the response to the first stimulus will interfere with the response to the second (Vince, 1948). This behaviour can be explained if humans operate as intermittent controllers (Craik, 1947, 1948). Intermittent controllers execute corrective responses in a serial ballistic manner and are subject to refractory periods (Telford, 1931; Pashler, 1994; Loram *et al.*, 2012). Once a corrective response has been executed, the controller will not respond to any further feedback for the duration of at least one refractory period. Refractoriness in humans is

believed to result from the inability to prepare two distinct responses simultaneously (Welford, 1952; Pashler, 1992). This limits the bandwidth of human manual control and explains that relatively slow rate of corrective actions.

Intermittent pulsatile control may confer certain advantages over more conventional continuous control. Loram *et al.*, (2010) investigated visuo-manual joystick control of an unstable load. Subjects either controlled in a conventional manner maintaining continuous contact with the joystick, or they controlled using gentle taps of the joystick. It was found that performance in the task was slightly superior when subjects controlled using taps. The authors suggested that control by gentle taps may allow for periods of higher quality feedback than control by continuous contact. Controlling with gentle taps means the subject is only intermittently in contact with the joystick. When not in contact with the joystick, sensory feedback is not corrupted by the subjects own motor noise. This may produce periods of enhanced sensory clarity allowing for more accurate disturbance rejection and improved performance. If this is true then sensory information is not constant but fluctuates depending its temporal proximity to motor outputs and control proceeds as an alternating epochs of action and sensation.

We aim to test this idea using a novel paradigm. We ask participants to balance a virtual unstable load through gentle taps of a joystick using only visual feedback. We block sensory information using brief visual occlusions (200 ms) at different instants relative to each tap. In some trials, the visual occlusions occur almost immediately after each tap (1 ms delay between taps and occlusions). In other trials, the occlusions are delayed for longer (up to 250 ms delay between taps and occlusions). We hypothesise that if control is broadly alternating between action and sensation, then blocking sensory information immediately

after each tap (i.e. being most concordant with a period of action) should be less disruptive than blocking sensory information during a period more likely to be associated with sensation processing (e.g. 200 ms after each tap).

Methods

Subjects and Ethical approval

20 healthy volunteers (12 male), aged between 18 and 57 took part in this experiment. Subjects gave written informed consent and the study was approved by the local human ethics committee and conformed to the principles of the Declaration of Helsinki.

Procedure

Subjects sat on a chair in a self selected position facing a 17 inch widescreen computer monitor positioned on a table approximately 80 cm in front of them (Fig 1). They held a small uniaxial joystick in their non-dominant hand and used their dominant hand to operate the joystick. Subjects also wore a pair of PLATO visual occlusion spectacles so that the presentation of visual information could be controlled precisely. The aim of the experiment was to keep the position of a real-time virtual load as close to the centre of the screen as possible through gentle taps of the joystick. The joystick position specified the torque input to the load. The position of the load was represented by the horizontal position of a red circle (3 cm diameter) displayed on the screen, and the centre of the screen was clearly marked by a white cross. Subjects were informed that deviation from the centre of the screen was a measure of performance. The vertical edges of the screen represented ± 8 degrees of inverted pendulum sway. Subjects always controlled the load through tapping so that each control action involved a discrete contact with the joystick. Each joystick contact

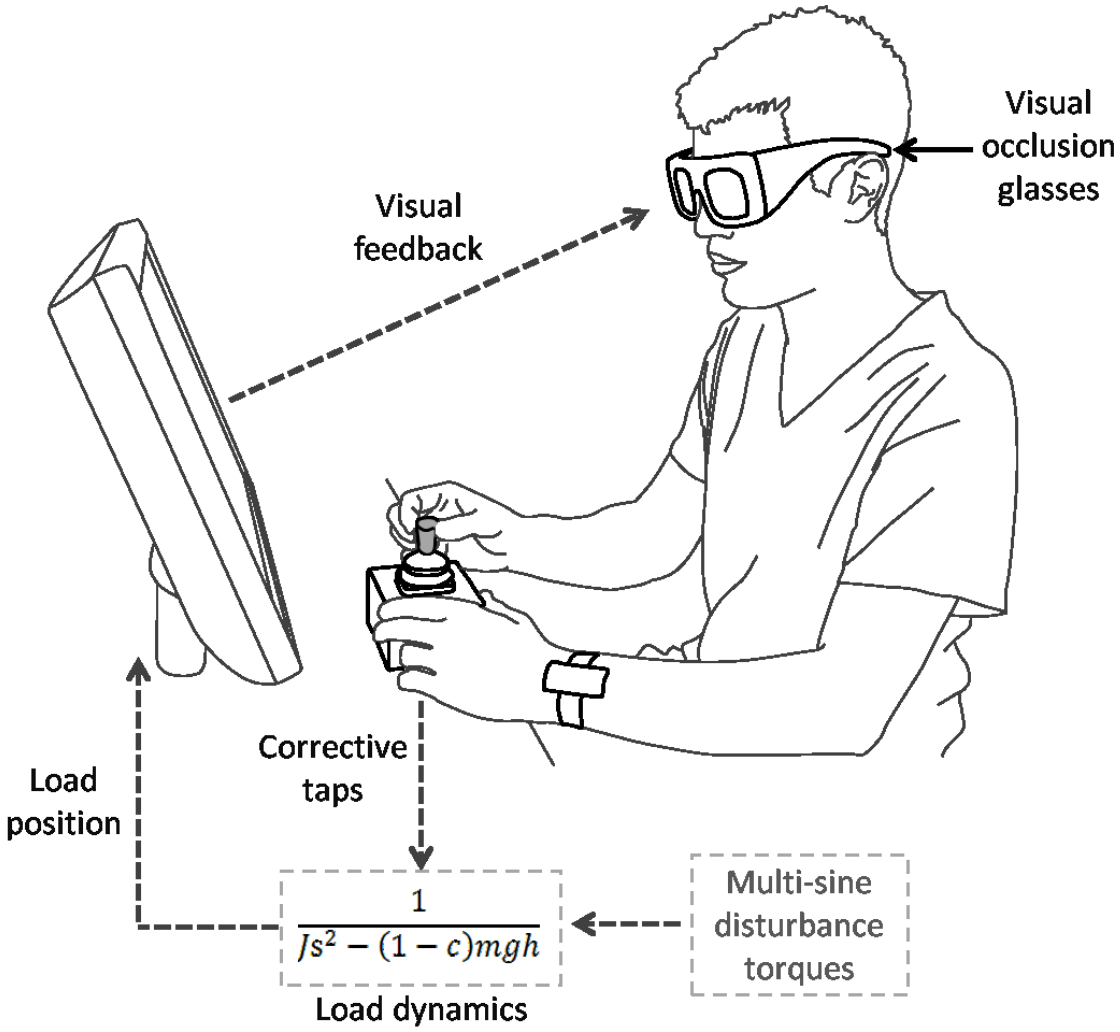

Figure 1. Experimental setup.

The subject balances a virtual unstable load through corrective taps of the joystick. They are compensating for a multi-sine disturbance signal that is continuously acting on the load. Visual feedback of load position is provided through a computer display. Visual feedback may be interrupted by brief (200 ms) occlusions using visual occlusion glasses. The subject is not in contact with the joystick but poised and ready to tap using either finger or thumb.

(each tap) produced a 5 V pulse for the duration of contact that was recorded in real time and could be used to trigger a brief visual occlusion.

As subjects performed the task, their vision was occluded for a period of 200 ms following each contact with the joystick. Within each trial, the delay between joystick contact and the 200 ms visual occlusion was constant. Between trials, the delay was varied among the following values: 1, 50, 100, 150, 200, 250, and 2000 ms. There was also a control condition where no occlusions were presented throughout the whole trial. Due to technical limitations the shortest duration between taps and occlusions was 1 ms but we consider this the 'immediate occlusion' condition. When there is a delay of 2000 ms (2 s) between taps and occlusions the temporal relationship between each tap and each occlusion is not clear to the subject. We consider this equivalent to a 'random occlusion' condition. We chose to use this delay instead of randomly presenting occlusions because it still links the number of taps with the same number of occlusions. Each of the 8 conditions was completed once for three virtual loads of varying stability which resulted in a total of 24 trials. Each trial lasted 120 seconds. As each trial required a high level of concentration, breaks were offered between trials and the experiment was split over two sessions that were separated by a minimum of 3 hours and a maximum of 1 week. At the start of each session subjects spent time familiarising themselves with the task and conducting a number of practice trials.

Real-time virtual loads

The real-time virtual loads were constructed using Simulink (Mathworks), compiled using Real-Time Workshop and executed on a laptop using Real-Time Windows Target within MATLAB 2011b at a sample rate of 1000 samples per second. All three virtual loads were modelled as unstable inverted pendulums described by the following transfer function:

$$\theta = \frac{T}{Js^2 - (1-c)mgh}$$

where θ is the angular position of the pendulum, T is the torque input, J is the moment of inertia, s is the laplace variable, m is the mass, g is the gravitational acceleration, h is the height of the centre of mass, and c is the stability ratio. The dynamics of the load were based on a model of a typical standing human - 'the human inverted pendulum' (Fitzpatrick & Taylor, 1992; Loram *et al.*, 2009*a*) where m = 70 kg, g = 9.81 ms^{-2}, h = 0.92. The moment of inertia (J) is given by kmh^2 where k is a shape factor of 1.3 (Morasso & Schieppati, 1999). The stability ratio (c) was varied among the following three values: 0.33 (low stability), 0.6 (medium stability) or 0.85 (high stability). As the stability ratio was always less than 1, all loads were unstable and would 'fall over' if no control was applied through the joystick. Changing the stability ratio altered the time constant of the pendulum given by:

$$\tau = \sqrt{\frac{J}{mgh(1-c)}}$$

which gave values of 0.43, 0.5, and 0.90 s in increasing order of stability. For an unstable pendulum, this time constant specifies the exponential growth rate of angle through time. A time constant of 0.90 s, which is the time constant of the load with a stability ratio of 0.85, is approximately equivalent to a human adult male inverted pendulum.

In each trial, an unpredictable torque disturbance was constructed and applied to the load. Subjects were required to compensate for the disturbance through taps to the joystick to prevent the load from falling over. The external disturbance was a multi-sine, of period 10 s, that contained power at frequencies 0.1, 0.2, 0.3 ... 10 Hz with a mean value of zero. The

disturbance amplitude was determined by preliminary experiments to make the task challenging but not frustratingly difficult. The disturbance amplitude was then kept constant for all trials.

In each trial the following signals were recorded: position (angle) of the virtual load; joystick position; joystick contact time; occlusion time. All signals were recorded at 1000 Hz and saved for subsequent analysis.

Data analysis

All data were analysed with MATLAB 2011b (Mathworks) using custom written scripts. In each individual trial we discarded the first 40 seconds of data to reduce the effect of any rapid familiarisation. We then identified the following: the interval between each tap; the instantaneous tapping frequency of each tap; the direction of each tap; and the performance over the whole trial. Individual taps were identified from the rising edge of each pulse in the joystick contact record. This method was suitable for identifying the great majority of taps but occasionally falsely identified a poor joystick contact as a succession of very quick taps. This problem was largely overcome in subsequent analysis (see smoothed histograms below). Once identified, the interval between each tap was calculated in milliseconds. The instantaneous frequency of each tap was defined as the reciprocal of tapping interval. The joystick position output, in combination with the tapping identification procedure was used to determine the direction of each tap. Performance was defined as the mean deviation of the load from the centre of the screen over the whole trial. The centre of the screen corresponded to the equilibrium point of the inverted pendulum (zero degrees). Thus, performance was calculated by rectifying the recording of load angle such that the direction of angular deviation was removed and only absolute values recorded. To assess

modal tapping frequency in each trial, tapping frequencies were binned (bin width 0.25 Hz) between 0 and 8 Hz, and the bin with maximum height determined the modal tapping frequency for that trial.

We wanted to investigate how the timing of visual occlusions impacted the distribution of tapping intervals. This was important because we hypothesised that the timing of the occlusions may impact on the level of disruption to tapping behaviour (being more concordant with sensation processing will be more disruptive). We found that tapping interval, as opposed to tapping frequency, was more intuitive to interpret in the context of the time domain defined visual occlusions. We created distributions of tapping intervals for each occlusion condition based on all 20 subjects' data. Tapping intervals were binned from 0 to 1000 ms (bin width 20 ms) which produced a conventional histogram for each condition (Fig 4 - grey bars). We also wished to estimate the modal tapping interval of each distribution with greater resolution. To do so, we created a smoothed histogram (Fig 4 – black line with transparent area). From each individual trial we calculated a conventional histogram (as above) and subsequently passed it through a zero phase low pass filter. This enabled calculation of the mean and 95 % confidence intervals for each visual occlusion condition in smoothed histogram form. Further to this we used cubic spline interpolation to estimate the peak of the mean smoothed histogram to a resolution of 1 ms. For a statistically robust estimate, the peak of the lower bound of the 95 % confidence interval was chosen to estimate the modal tapping interval in each condition. This method confers the additional benefit of largely filtering out any spurious peaks in the conventional histograms. For example, a poor contact of the joystick occasionally resulted in the false

registration of several implausibly rapid taps. The smoothed histogram method reduces the impact of these erroneous measures.

Statistical analysis

Statistical analysis was conducted using MATLAB 2011b (Statistics Toolbox). A two-way ANOVA was used to test for effects of stability and occlusion timing on the chosen dependent variable (tapping frequency or performance). Where no significant interaction was found between stability and occlusion timing, the main effects of stability or occlusion timing on the chosen dependent variable were deemed appropriate to interpret. A one-way ANOVA was used to test for the effect of occlusions on performance in additional experiments. Post-hoc comparisons were conducted using the Tukey-Kramer correction. We also repeated the statistical analysis using equivalent non-parametric tests (Friedman and Kruskal-Wallis) and found identical results. Unless otherwise stated, individual values are presented as mean ± standard deviation. All box plots show the median (central mark in box), 25th and 75th percentiles (edge of box), mean excluding outliers (asterisks) and most extreme data points not considered outliers (whiskers). All outliers are plotted individually. Outliers were calculated as:

$$q \pm w(IQR)$$

where *q* is either the 25th or the 75th percentile, *w* is the maximum whisker length set at 1.5, and *IQR* is the interquartile range.

Additional experiments

6 volunteers participated in a set of additional experiments. All subjects gave written informed consent and the study was approved by the local human ethics committee and

conformed to the principles of the Declaration of Helsinki. In these experiments the length of occlusion was set at 125 ms as opposed to 200 ms which was used in the original experiments. We chose this length based on the results and interpretation generated from the main experiments (see discussion for rationale). There were four conditions: control, 1 ms delay, 125 ms delay, and 2000 ms delay. In the control condition no occlusions were presented. The other conditions denote the delay between the tap and the subsequent occlusion. All 6 subjects completed each of the four conditions three times.

Results

Figure 2 shows a ten second representative trace of a subject balancing the 85 % stable load via gentle taps of the joystick. The pendulum position is shown in Figure 2A. As is clear in this example, the pendulum tends to sway back and forth over the equilibrium point (zero degrees) as the subject attempts to keep the load as central as possible. Typically, when the load is swaying close to the equilibrium point, the direction of the taps alternate (Fig 2A, 18-20 seconds – each tap is marked by a black triangle and the direction of the triangle denotes the direction of the tap). When the load moves further from the equilibrium point, multiple unidirectional taps are observed (Fig 2A, 21-23 seconds). The accompanying joystick position trace is shown in Figure 2B. This corresponds to the virtual force that is applied to the load. Each tap (again marked by black triangles) results in an abrupt joystick movement characterised by a damped oscillation due to joystick dynamics. The resulting virtual torque impulse changes the velocity of the load. In this example, each tap also triggered a 200 ms visual occlusion. This is shown in Figure 2C. Here, the brief moments when the subject was in contact with the joystick (i.e. during each tap) are shown by the dashed black line rising above 5 V. The consequent visual occlusions are denoted by the full grey line rising above 5

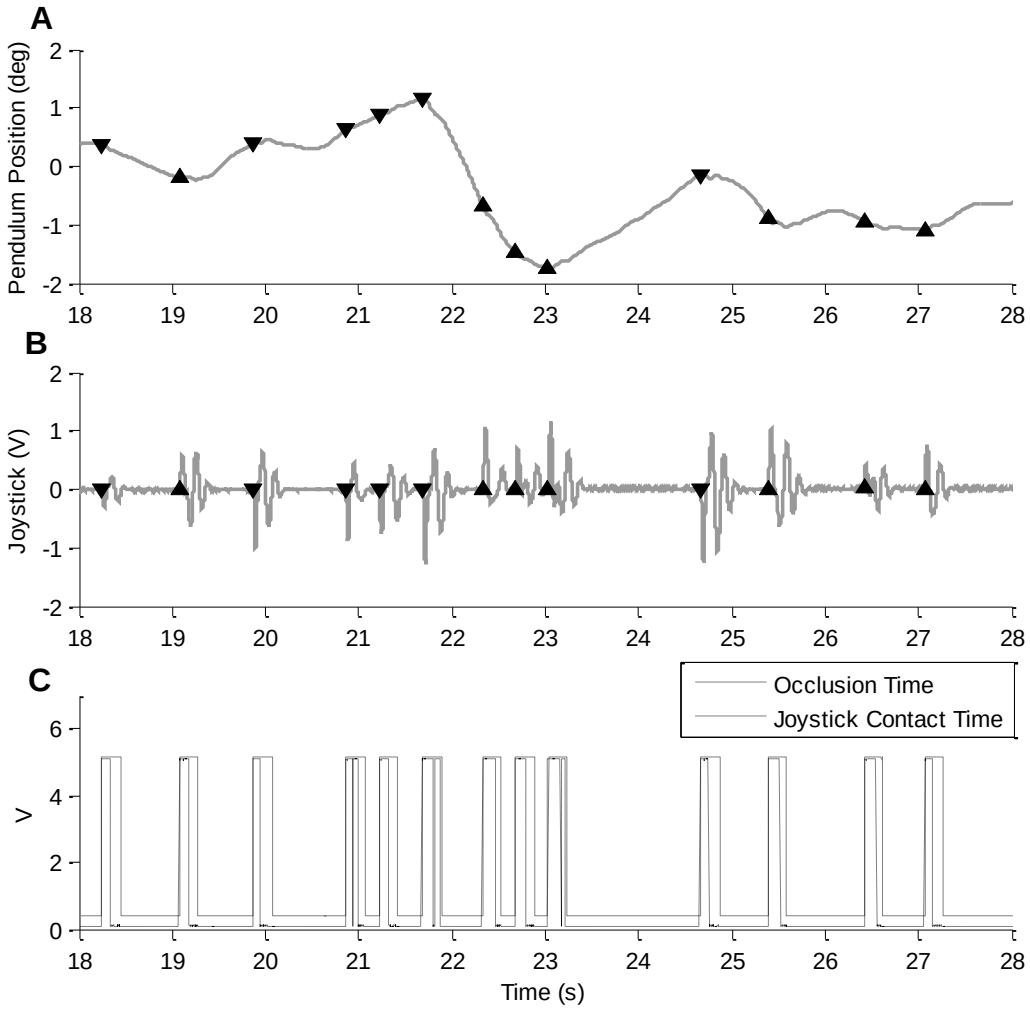

Figure 2. Representative trace.

A, shows the position of the load in degrees. Each black triangle marks a tap. The direction of the taps is denoted by the direction of the triangle. B, shows the joystick position (units in volts). Again, each black triangle marks a tap and the direction is shown by the direction of the triangle. C, shows joystick contact time (dashed trace), and visual occlusion time (solid line). During contact with the joystick, this line rose above 5 volts. The visual occlusions are shown by the solid line exceeding 5 volts. In this trial the delay between taps and occlusions is 1 ms.

V. As can be seen, the duration of each visual occlusion was always constant (200ms) despite the fact that the contact time with the joystick was variable. In this example, the delay between each joystick contact and each visual occlusion was 1 ms so that each tap of the joystick was accompanied by an (almost) immediate visual occlusion.

We first wanted to know whether load stability had an impact on modal tapping frequency. All loads were unstable but varied in their degree of instability: the time constants for the lowest, medium and highest stability loads were 0.43, 0.5, and 0.9 s respectively. A two-way ANOVA was conducted to uncover any interaction between load stability and occlusion timing. No significant interaction was found ($p = 0.613$) so we considered the grand modal tapping frequency at each load stability including all visual occlusion conditions. Figure 3 shows box plots of the modal tapping frequency for each of the three load stabilities over all experimental conditions. The results of the 2 way ANOVA showed a small but statistically significant main effect ($p < 0.01$) of load stability on tapping frequency. Post hoc pair-wise comparisons revealed that the modal tapping frequency in the highest stability condition was lower than in the lowest stability condition (1.66 ± 0.51 Hz vs 1.86 ± 0.63, $p < 0.05$). There were no significant differences between the medium stability condition (1.75 ± 0.47 Hz), and the high or low stability conditions.

We next considered how tapping frequency might be affected by visual occlusions. In particular, we wanted to know how the timing of the visual occlusions might affect the tapping interval. Figure 4 shows histograms of mean tapping intervals from the lowest stability condition. There are 8 different subplots, each of which shows data from a different visual occlusion condition. Each subplot shows a standard histogram (grey bars), and a smoothed histogram ± 95 % confidence intervals (thick black line and grey area – see

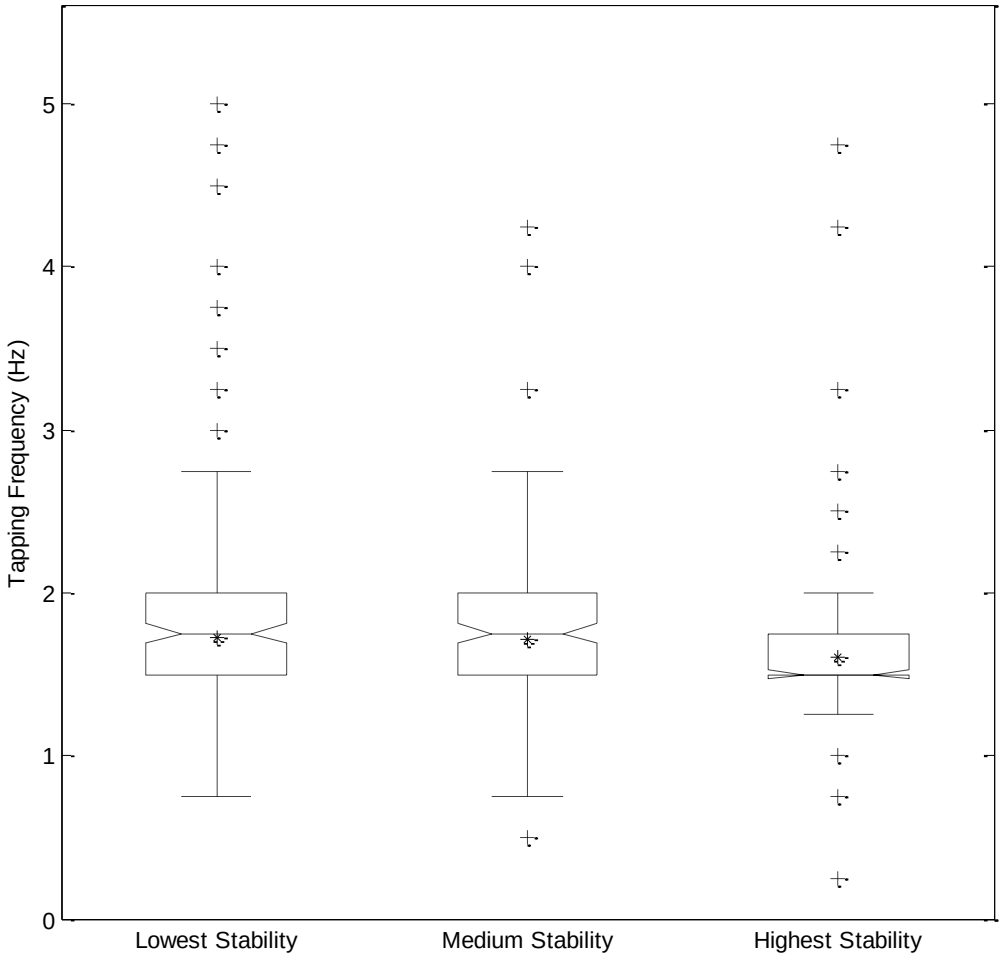

Figure 3. Modal tapping frequency for different load stabilities.

Box plots of modal tapping frequency with all data pooled from each trial at different stabilities. Box plots show median (central mark in box), 25th and 75th percentiles (edge of box) and extreme data points (whiskers). Outliers are plotted individually (crosses). The mean (excluding outliers) is also plotted (asterisk).

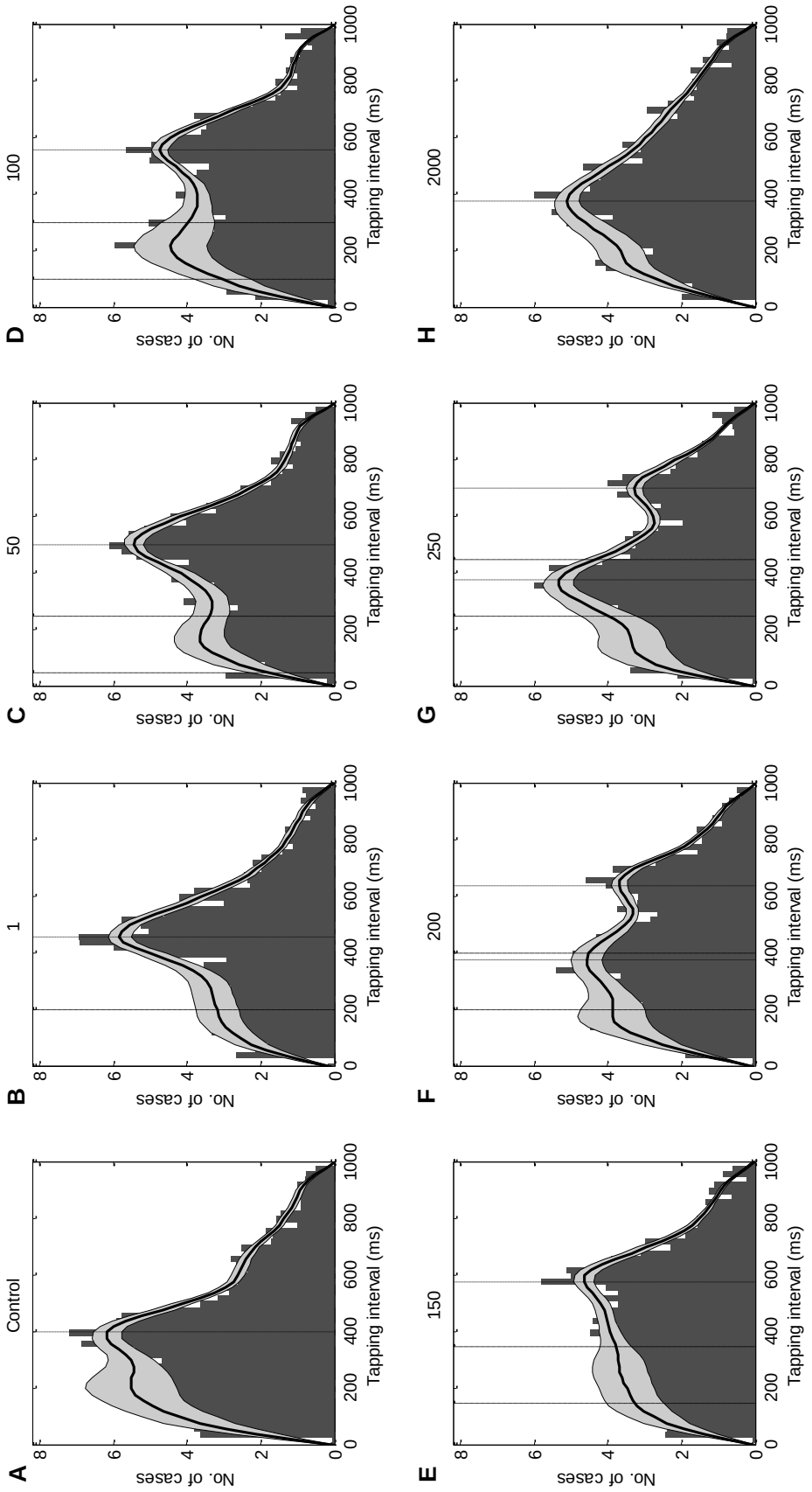

Figure 4. Histograms of tapping intervals for different visual occlusion conditions. Each plot shows a traditional histogram (grey bars) and a smoothed histogram ± 95 % confidence intervals (black like with grey surround) of tapping interval for each visual occlusion condition. All data are from the lowest stability load. A, shows the control conditions where no visual occlusions were presented. B-H show visual occlusion conditions. The delay between each tap and the presentation of the visual occlusion is shown by the label above each plot (e.g. C = 50 ms delay). The timing of the visual occlusions is shown by the area between the two dashed lines in each plot. Modal tapping intervals are estimated from the lower bound of the 95 % confidence intervals of the smoothed histograms.

methods for details). The peak of the lower bound of the 95 % confidence interval is used to give a statistically robust estimate of the mean modal tapping interval of all subjects. Figure 4A shows the control condition where no visual occlusions were presented. There are two peaks in the distribution. One occurs at an interval of around 200 ms, and the next occurs at an interval of 391 ms. The first peak is accompanied by wide confidence intervals which suggests that this particularly fast tapping interval was not common to all subjects in this condition. The second peak has substantially narrower confidence intervals and the modal tapping interval is identified here (vertical dotted line). Thus, when balancing the most unstable load with no visual occlusions, subjects were most likely to tap every 391 ms (instantaneous frequency = 2.56 Hz). Subplots B-H show the visual occlusion conditions. The top of each subplot is labelled to denote the delay between the taps and the occlusions. In Fig 4B, the delay between the taps and occlusions was 1 ms. The timing of the occlusion is also represented in the plot by the two parallel vertical dashed lines (in plot B between 1 and 201 ms). The modal tapping interval in this condition (plot B) is clearly defined by a sharp peak in the distribution at 465 ms (vertical dotted line). This is 264 ms after the end of the visual occlusion. In Fig 4C, where the delay between taps and occlusions was 50 ms, the modal tapping interval shifted to 502 ms: 252 ms after the end of the visual occlusion. This consistent relationship, where the modal tapping interval occurs approximately 250 ms after the end of the visual occlusion, was maintained up until the delay between taps and occlusions reaches 200 ms (Fig 4F). This is best seen visually in Fig 4B-E. Note that the gap between the end of the visual occlusion (vertical dashed line), and the peak in the tapping distribution (vertical dotted line) remains almost constant. In Fig 4F, the pattern is broken: the modal tapping interval is identified at 375 ms. This is similar to the result observed in the control condition (Fig 4A – 391 ms) as opposed to the 650 ms (200 + 200 + 250 ms) that

would be predicted from plots B-E. However, a secondary peak is present in subplot 4F at 644 ms. In subplot 4G the delay between taps and occlusions is 250 ms. Here, the distribution follows a similar pattern to that of subplot 4F, but the first peak (at 371 ms) is more pronounced. Once more there is a secondary peak approximately 250 ms after the end of the visual occlusion (696 ms). When the delay between taps and occlusions reaches 2000 ms (Fig 3H), this bimodal distribution disappears and there is a clear single modal tapping interval at 384 ms. Thus, we observed two common tapping intervals. One occurred at 380 ± 9 ms when, either there were no visual occlusions or there was at least 200 ms of vision available following each tap (Fig 4A, F, G, H), and the second occurred 249 ± 11 ms following the end of a visual occlusion (Fig 4B-G).

This pattern of results was repeated in the medium and highest stability conditions. The modal tapping intervals for each of the three loads, and each visual occlusion condition are shown in Table 1. Where the distributions were bimodal, the location of both peaks is shown. In the medium stability condition, the two common tapping intervals were 393 ± 24 ms and 264 ± 13 ms. In the highest stability condition the two common tapping intervals were 402 ± 23 ms and 277 ± 15 ms.

We also wanted to know whether the timing of the visual occlusions would have an impact on performance. A two-way ANOVA was conducted to examine the effect of stability and occlusion condition on performance. No significant interaction was found between the effects of stability and visual occlusion timing ($p = 0.55$). Significant main effects were found for both stability ($p < 0.001$) and visual occlusion timing ($p < 0.001$). Post-hoc pair-wise comparisons revealed that mean performance in the lowest stability condition (1.06 ± 0.34 deg), the medium stability condition (0.74 ± 0.27 deg) and the high stability condition (0.49

	Control	1 ms	50 ms	100 ms	150 ms	200 ms	250 ms	2000 ms
Lowest Stability	391	465	502	556	583	375 644	371 696	384
Middle Stability	367	483	525	565	598	403 654	382 710	422
Highest Stability	372	492	547	564	618	425 679	398 712	413

Table 1. Modal tapping frequency in each condition.

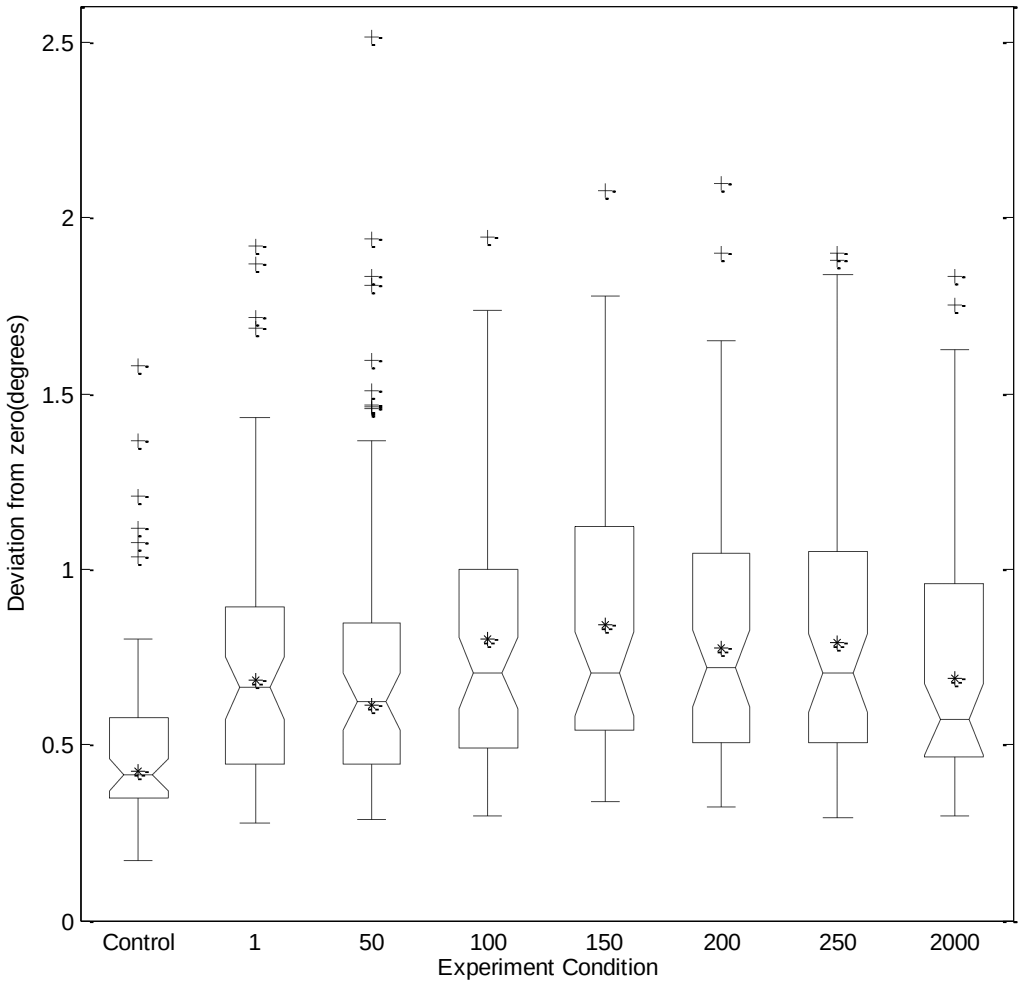

Figure 5. Effect of occlusion timing on performance.

Box plot of performance in each occlusion condition. Experiment condition (x-axis) denotes the delay between taps and occlusions. Each plot shows the mean deviation from zero in each condition. Box plots show median (central mark in box), 25th and 75th percentiles (edge of box) and extreme data points (whiskers). Outliers are plotted individually (crosses). The mean (excluding outliers) is also plotted (asterisk).

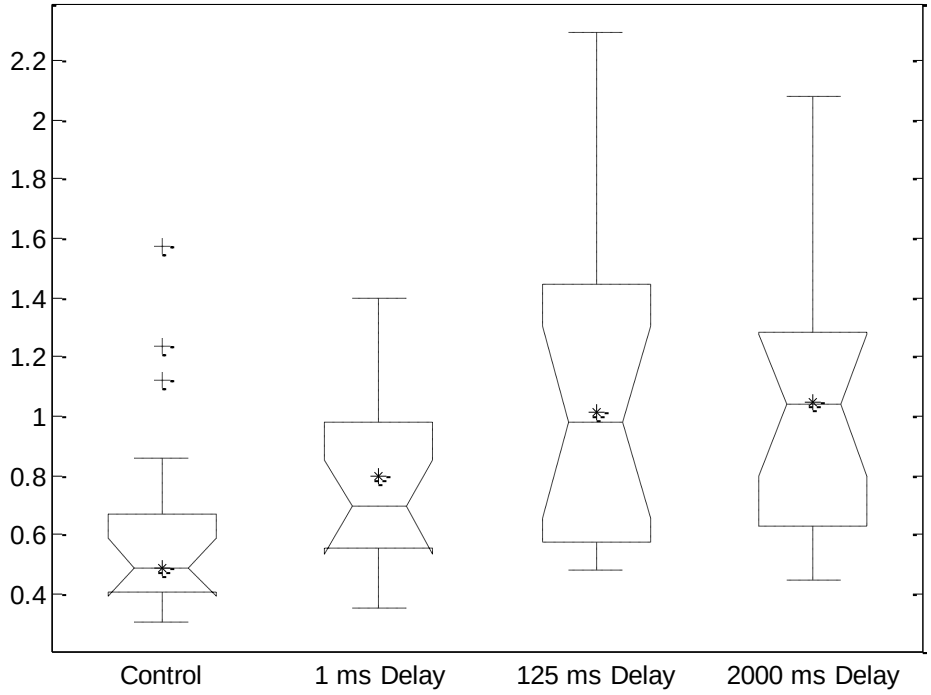

Figure 6. Results from additional experiment: effect of occlusion timing on performance.

In a separate experiment the occlusion length was set at 125 ms. Experiment condition (x-axis) denotes the delay between taps and occlusions. Each plot shows the mean deviation from zero in each condition. Box plots show median (central mark in box), 25th and 75th percentiles (edge of box) and extreme data points (whiskers). Outliers are plotted individually (crosses). The mean (excluding outliers) is also plotted (asterisk).

deg ± 0.11 deg) were all significantly different from one another. We were most interested in the effect of visual occlusion timing on performance. These results are plotted in Figure 5. These plots are made up of grand averages from all stability conditions. Pair wise comparisons revealed that performance was significantly impaired in all visual occlusion conditions when compared with the control condition. The plot suggests that performance was most impaired when the visual occlusion was presented after at least 100 ms although this observation is not justified statistically.

Figure 6 shows the results of the additional experiment. Here, the length of the occlusion was 125 ms and the delay between tapping and the occlusion was varied between 1 ms, 125 ms and 2000 ms. There was also a control condition with no occlusions. We wanted to know whether the timing of a shorter visual occlusion would have a measurable impact on performance. A one-way ANOVA revealed significant differences between conditions in these experiments. Post-hoc, pair-wise comparisons showed that performance was significantly impaired compared with the control condition when the occlusion was presented with a delay of 125 ms ($p < 0.05$) or with a delay of 2000 ms ($p < 0.05$). There was no statistical difference between the control condition and the immediate occlusion condition ($p = 0.11$).

Discussion

In human manual control corrective actions proceed at a fairly sluggish rate of two to three per second (Vince, 1948; Lakie *et al.*, 2003; Lakie & Loram, 2006; Loram *et al.*, 2006*a*, 2010) despite the fact that voluntary movements can be made with much higher frequency (Loram *et al.*, 2006*a*). This limited rate of corrective action has been found to persist in the face of large changes in load dynamics (Lakie *et al.*, 2003; Loram *et al.*, 2006*a*). The results of

the current experiment extend these findings to control by gentle taps. Figure 3 shows box plots of the modal tapping interval of all subjects for the three different load stabilities. The load stability refers to the time constant of the virtual inverted pendulum: the rate at which the load 'falls over'. Intuitively it might be predicted that the modal tapping frequency should increase for a lower stability load to compensate for faster load dynamics. This is not what we found. Modal tapping intervals were remarkably consistent despite the fact that the time constant was altered by a factor of two between the lowest and highest stability loads (0.43 s vs. 0.9 s). Although we observed a statistical difference between the mean modal tapping interval of the highest (1.66 ± 0.51 Hz) and lowest stability loads (1.86 ± 0.63 Hz), we consider the similarity to be far more striking than the difference. The data strongly suggest that manual control by gentle taps is subject to the same bandwidth limitations and refractoriness (Vince, 1948; Loram *et al.*, 2012) as other types of manual control.

In order to balance the load regular corrective action is required because without intervention, or with randomly applied forces, the load will simply fall over. The relative invariance of tapping interval to load dynamics, and strong agreement with previous work, implies that the modal tapping interval reveals an intrinsic property of the human neural controller. The human is producing taps with a clear preferred rate of action. To aid interpretation of the experimental results we present a conceptual model of tapping control in Figure 7. In this model each tap marks the start of a new control cycle (Fig 7-1 first arrow). When vision is not occluded, feedback is available for the duration of the control cycle, and is used to evaluate the state (position and velocity) of the load in order to construct the next corrective motor output. The motor output is then executed and the cycle restarts. Thus,

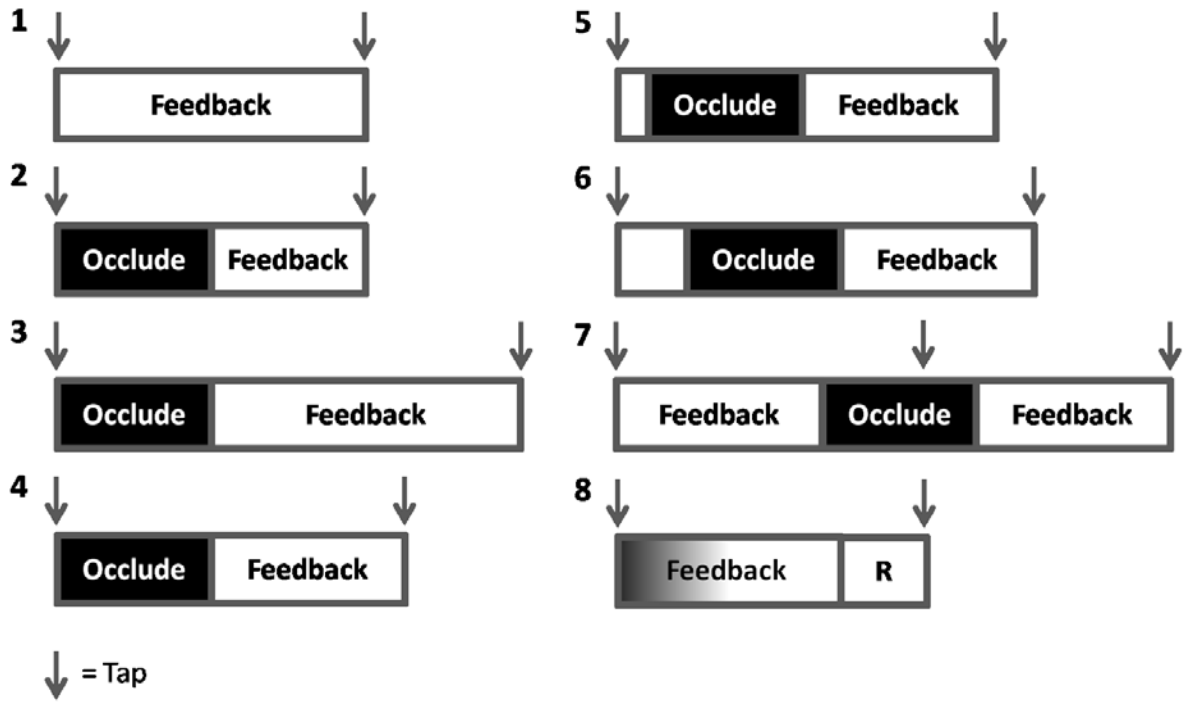

Figure 7. Conceptual model of tapping control.

Tapping control proceeds in 'control cycles'. Each control cycle begins and ends with a tap such that the duration of each control cycle is equal to the duration between two taps. Under normal conditions feedback is available for the duration of each control cycle. In this experiment, we blocked sensory feedback (through visual occlusions) at different points in each control cycle. Details of each diagram are provided in the text.

the duration of each control cycle is simply the time in between two consecutive taps. This is analogous to the 'drop and catch' process described by Loram *et al* (2001).

We attain a deeper insight into this process by looking at the distribution of tapping intervals. Figure 4A shows a histogram of tapping intervals when vision is uninterrupted. A smoothed histogram (black line with light grey surround) representing the mean ± 95 % confidence intervals is plotted on top of a traditional histogram (grey bars). Tapping rate may be presented in terms of frequency (Hz) or in terms of tapping interval (ms). Here we choose tapping interval as it allows the histogram to be interpreted in the context of a control cycle. The cycle begins with a tap at time zero and the next tap can occur any time in the next 1000 ms (we recorded very few tapping intervals greater than one second). The height of the histogram estimates the probability of tapping at any instant over that one second period. In this condition with no visual occlusions subjects were most likely to tap after 391 ms (peak of the distribution – identified by the vertical dashed line (--)). However, tapping clearly occurred over a wide range of intervals. In particular there is a shoulder in the distribution at around 200 ms, which means that taps could occur rather quickly. Visual inspection reveals that this faster rate is often associated with multiple unidirectional taps (e.g. Fig 2A , 21 – 23 seconds). The wide confidence intervals also show that this feature was not common to all subjects. These data compare well with previous work where slow (≈ 450 ms), and faster (≈ 200 ms) modes of tapping were identified (Loram *et al.*, 2010). Thus, an average control cycle lasted between 350 and 450 ms, but at times some subjects also briefly adopted a faster tapping interval around 200-250 ms.

Under normal conditions visual feedback is available for the entire duration of each control cycle (Fig 7-1 - white 'feedback' block between the two arrows). The key manipulation in

this experiment was blocking sensory feedback during different parts of the control cycle. In doing so, we hoped to reveal whether feedback was more important during certain parts of the control cycle than during others. Specifically, we hypothesised that sensory feedback would be least useful during the very first part. At one extreme, if sensory feedback is redundant for the first half of a control cycle, a sensory blockade of this period will have no effect. This is depicted in Figure 7-2 where an immediate occlusion has no impact on the length of the control cycle. At the other extreme, the full duration of sensory feedback is required to elicit the next motor response. This is depicted in Figure 7-3 where the interval between two taps is the sum of the occlusion length and one normal control cycle length. If the reality is between these two extremes, then the extent to which the occlusion lengthens the control cycle should provide an estimate of the period of 'sensory redundancy'. By sensory redundancy, we mean a period of time for which sensory feedback has limited or no use. For example, if an immediate 200 ms occlusion only extended the control cycle by 100 ms, then the occlusion has only interrupted 100 ms worth of sensory feedback. In this case, we would suggest that the first 100 ms of sensory feedback is largely unused or 'redundant'.

Figure 4B shows a histogram of tapping intervals when a 200 ms visual occlusion immediately followed each tap (in reality there was a 1 ms delay between each tap and occlusion but we refer to this as an immediate occlusion). The visual occlusion is represented by the area between time zero on the x-axis and the vertical dashed line (— —) at 200 ms. Thus in this condition subjects are deprived of sensory feedback for the first 200 ms of each control cycle. If, under normal un-occluded conditions, the first 200 ms of sensory feedback is not normally used, then we would expect the tapping histogram to remain unchanged by the manipulation. A quick comparison between the control condition

(Fig 4A) and this condition (Fig 4B) reveals this is not the case. One difference between Fig 4B and 4A is the reduction in faster tapping intervals at around 200 ms. This probably reflects the penalty of tapping this frequently when each tap produces an occlusion. The most interesting difference between this condition and the control condition is that the peak of the distribution in Figure 4B has shifted to the right by 74 ms (from 391 to 465 ms). This is depicted schematically in Figure 7-4. The shift in modal tapping frequency is quite small and is more similar to the hypothesis presented in Figure 7-2 than Figure 7-3. This suggests that the visual occlusion is only interrupting 74 ms worth of feedback. We can therefore speculate that the sensory feedback remains largely unused for the first 126 ms of each control cycle.

Figures 4C – G show the effect of shifting the visual occlusion to different stages in the control cycle. The delay between taps and occlusions is shown above each plot in units of milliseconds. The timing of the visual occlusion is also represented visually as the time between the two vertical dashed lines (— —). The modal tapping interval (peak in the distribution) in each plot is marked by the vertical dotted line (--). Modal tapping intervals for all conditions are also presented numerically in table 1. The timing of the visual occlusion has a clear and consistent relationship with the modal tapping interval. In Figure 4 B-H there is a clear peak in each histogram 249 ± 11 ms after the end of the visual occlusion in every plot. The medium and high stability conditions revealed a very similar effect: they showed a clear peak in each histogram 264 ± 13, and 277 ± 15 ms after the end of the occlusion for each load respectively. For each load, the intervals of 249 ± 11, 264 ± 13, and 277 ± 15 ms represent the most common response time between the availability of visual feedback (the end of the occlusion) and the subsequent tap. The intervals are remarkably consistent. Upon

cessation of the occlusion, subjects prefer to wait for a fixed time that is considerably longer than the minimum feedback time delay in this task (Loram *et al.*, 2010) before making the next corrective response. This interval remains unaltered regardless of the position of the occlusion in the control cycle. This is shown schematically in Figure 7-4 – 7-6. Such remarkable consistency suggests that this interval represents an optimum response time between the presentation of visual feedback and the subsequent tap. This optimum response time (≈ 250 ms for low stability load) is considerably shorter than the modal tapping interval (391 ms) observed under control conditions. This difference may be resolved if each control cycle begins with a period of sensory redundancy which is then followed by an average response time of 250 ms.

One final observation may be made from the histogram plots. The ≈ 400 ms modal tapping interval that is observed under control conditions (Fig 4A) is restored when the occlusion begins 200 ms or later in the control cycle (Fig 4F – G). This is illustrated in Figure 7-7. This reveals the quantity of uninterrupted visual feedback required immediately following a tap to produce this preferred tapping rate. It is first evident in Figure 4F when 200 ms of visual feedback followed each tap before the onset of an occlusion. Interestingly it is more prominent when 250 ms of immediate feedback is allowed (Fig 4G). A clear pattern emerges: an increasing dominance of a peak at around 400 ms paralleled with the decline in the second peak that follows the end of the occlusion. It seems likely that the normal (un-occluded) pattern of tapping distributions would be restored if the occlusion began 300 to 350 ms into the control cycle. This is indeed the case when there is a substantial delay between taps and occlusions (Fig 4H, 2000 ms delay). In Figure 4G where the normal pattern is nearly restored, the majority of taps occur while the subject is occluded. There is a period

between 250 to 400 ms where the subject has no visual feedback but has not yet made contact with the joystick. This period is presumably associated with both response planning and response execution. There is a large body of evidence showing that humans can only plan one response at a time (Welford, 1952; Pashler, 1992, 1994). This response planning bottleneck is often referred to as the psychological refractory period and is believed to explain the relatively slow bandwidth of human voluntary control (Vince, 1948; Loram *et al.*, 2012). Thus, we suggest that the psychological refractory period would theoretically be positioned in this section of our conceptual model but full discussion is beyond the scope of this chapter.

We may summarise our observations thus far with an updated model of an un-occluded control cycle. This is shown in Figure 7-8. The control cycle begins with a tap. Immediately following this tap is a period of sensory redundancy (≈ 125 ms in the low stability condition) that fades over time (denoted by the fading grey in the feedback block). As the sensory redundancy is fading, sensory clarity is increasing (white portion of feedback block). Once enough feedback has been accumulated, there is a further period associated with response planning and response execution (shown by the box labelled 'R') before the control cycle ends when the joystick is contacted with the next tap.

This simple model allows us to make some predictions regarding performance in the task. All subjects were instructed to keep the inverted pendulum sway as small as possible, and as such, average deviation from zero gives a measure of performance: the further from zero the worse the performance. Given our conceptual model, we would predict that those trials in which visual occlusions were most concordant with the period of 'sensory redundancy' should impair performance the least. In contrast, those trials where visual occlusions were

more aligned with the period of sensory clarity should impair performance the most. Figure 5 shows performance data pooled from all load stabilities over different occlusion conditions. Each occlusion condition is labelled on the x-axis by the delay between taps and occlusions in units of milliseconds. Performance in all visual occlusion conditions was significantly worse than performance in the control condition. While there is no statistical difference between any of the visual occlusion conditions, the pattern of results are consistent with the conceptual model. Performance in the 1ms and 50 ms delay conditions does not appear as badly affected as in the 100, 150, 200 and 250 ms conditions. It is likely that the effect of occlusion timing on performance was somewhat washed out because, at 200 ms, the occlusion is longer than our own estimations of the period of sensory redundancy.

In order to test our hypothesis more rigorously we conducted some additional experiments. For the low stability load, we estimated that the period of sensory redundancy is around 125 ms. We therefore repeated the experiments using this load, but with a sensory occlusion length of 125 ms. The occlusion was presented either almost immediately in the control cycle (1 ms delay), after a delay of 125 ms, or after a delay of 2000 ms. Performance data from these experiments are presented in Figure 6. We found that performance was significantly degraded when the occlusion was delayed by 125 ms or 2000 ms. When the occlusion was presented immediately (labelled 1 ms delay), and therefore concordant with the estimated period of sensory redundancy, performance was not statistically different from the control condition. In addition, we found that the control cycle length in this condition was 401 ms which is very similar to that of the control condition. These data are highly consistent with our conceptual model in Figure 7-8.

Control by tapping means the subject is only intermittently in contact with the joystick. A tap will cause a short impulse to act on the load. Once this impulse is complete, the only forces acting on the load are gravity and external disturbances. This unambiguously separates the effects of motor actions (taps) from the effects of external forces (disturbance and gravity). This period of separation should allow for a greater understanding of the statistical properties of the disturbance and a clearer estimate of load dynamics. The current data support this theory. We show evidence that the usefulness/quality of sensory feedback is lower immediately following each tap, but quickly rises thereafter. This suggests that subjects are broadly alternating between action and sensation.

We also contend that this explains why performance with gentle taps was shown to be slightly superior to performance with continuous contact (Loram *et al.*, 2010). Control with continuous contact does not allow such unambiguous separation of motor outputs from other forces acting on the load. However, even when controlling with continuous contact, humans still use discrete pulsatile actions (Lakie *et al.*, 2003; Lakie & Loram, 2006; Loram *et al.*, 2006*a*, 2009*a*, 2010). This mode of control should still allow for improved differentiation between motor output and external disturbances forces compared with a conventional continuous controller. Indeed, any control strategy of this type should create distinct periods of motor output separated by periods of greater sensory clarity. This is further supported by strong evidence that sensory feedback is actually attenuated during active movements (Collins *et al.*, 1998; Seki *et al.*, 2003).

Do the current observations have any relevance to the control of quiet standing? Loram *et al.*, (2005) used dynamic ultrasonography to show that, during quiet standing, the calf muscles operate in a pulsatile manner that is strikingly similar to manual balancing of an

unstable inverted pendulum (Lakie *et al.*, 2003). These similarities have led some authors to propose that quiet standing control is achieved through serial ballistic control (Loram *et al.*, 2009*d*). Thus, it is plausible that control of quiet standing proceeds as a series of 'gentle taps' by the calf muscles as a means to overcome ambiguous sensory feedback (Loram *et al.*, 2009*c*), and to compliment attenuation of sensory feedback that occurs during active movements.

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Chapter 6

GENERAL DISCUSSION

Discussion

In this thesis we have presented four experimental chapters that all relate to the neural mechanisms of human balance control. In our first experimental chapter, we developed a new automatic tracking technique that is appropriate for analysing ultrasound videos of the human calf muscles. This is particularly useful for investigations into quiet standing control. In the second experimental chapter, we applied this technique to study the sensitivity of the human balance control system. Contrary to our initial expectation, we found that afferent sensors were able to detect and respond to tiny perturbations to stance that were considerably below the size and speed of normal sways. In the third experimental chapter we focussed on the relative contribution of reflex and higher level pathways to a balance control task that is similar to standing. To explain the results of our experiments we developed a simple computational model of balance where control is dominated by higher level pathways but supplemented by reflexes. In our final experimental chapter we focussed on the role of sensory feedback during higher level visuo-manual balance control. We suggested that a conceptual model where control proceeds as alternate periods of action and sensation provides the most satisfactory explanation for our data, and we discussed potential implications for the control of quiet standing. We now discuss how the studies presented in this thesis contribute to our current understanding of human balance control.

While many researchers propose that balance control is achieved through reflexes (Deliagina *et al.*, 2007; Lockhart & Ting, 2007), others propose this is unlikely in part because

the size and speed of sways during quiet stance are below the threshold of peripheral reflex mechanisms (Loram *et al.*, 2005*c*, 2009*a*). One model of quiet standing control has been specifically formulated on this basis (Bottaro *et al.*, 2008). It is true that the vast majority of research that supports the reflex concept of balance control has been conducted using quite large perturbations that elicit clear reflex responses (Nashner, 1976; Diener *et al.*, 1984; Gollhofer *et al.*, 1989; Peterka, 2002; van der Kooij & de Vlugt, 2007; Welch & Ting, 2008), and it does not necessarily follow that these stereotyped responses to such large perturbations should apply to quiet standing control. Some studies have also argued that detection of small sways is complicated by short range muscle stiffness (Loram *et al.*, 2007*b*, 2009*c*) and paradoxical muscle movements (Loram *et al.*, 2004). Paradoxical muscle movements complicate the task of extracting useful information regarding sway from muscle and force afferents (Loram *et al.*, 2009*c*). These ideas are also supported by psychophysical evidence of conscious sway detection (Fitzpatrick & McCloskey, 1994).

Experiments that have applied small ankle joint perturbations during sitting (Evans *et al.*, 1983) or standing (Gurfinkel *et al.*, 1995) tend to support the view the reflex mechanisms have quite a high threshold. However, the analysis of such experiments is challenging. It is not always clear whether small perturbations fail to elicit a response, or whether the experimental methods have failed to detect a response that is convincing enough to report. Electromyography in particular is quite a noisy measurement technique which can make small responses difficult to interpret (Clancy *et al.*, 2002). Recently, using automatic tracking algorithms, it has become possible to make in vivo measurements of changes of muscle contractile length (Loram *et al.*, 2005*c*, 2007*b*; Lakie & Loram, 2006; Osborne & Lakie, 2011).

These measurements have a superior signal to noise ratio to EMG and provide an additional means to measure small muscle responses.

Using the methods developed in the first experimental chapter of this thesis, in combination with more conventional techniques, we have been able to readdress the question of sensory thresholds in human standing. As described in the second experimental chapter, we perturbed standing subjects using a low velocity support surface tilt, much like Gurfinkel *et al.*, (1995), such that the normal balance process remained largely uninterrupted. We measured calf muscle responses using EMG and dynamic ultrasonography in an attempt to determine the point at which the nervous system first detected and responded to this tiny perturbation. We were surprised by the result. Our observations revealed a highly sensitive low threshold neural mechanism of balance control.

For a number of reasons we believe that this highly sensitive mechanism is probably reflexive in origin. Firstly, the response we observed was actually inappropriate and destabilising which is not a hallmark of higher level computation. Indeed, faster platform rotations have been consistently shown to initially trigger medium or long latency destabilising reflex responses (Nashner, 1976; Diener *et al.*, 1984; Gollhofer *et al.*, 1989; Loram & Lakie, 2002*b*). Secondly, the response that we measured occurred well below reported values of conscious perception (Fitzpatrick & McCloskey, 1994) which seems more consistent with a reflex rather than higher level response. Finally, authors who have devised a theoretical model of balance control have found that experimental data are best explained when the model contains a local proprioceptive reflex loop with no threshold (Mergner *et al.*, 2005; Mergner, 2010). Although we feel there are problems with this approach (if the model is an inappropriate representation of the true control mechanisms then

interpretation of such findings is difficult) we note that these ideas are consistent with our data. We therefore conclude that normal human balance control proceeds with a highly sensitive neural control component that is probably reflexive in nature. What are the implications of this conclusion?

Firstly, we suggest it is inappropriate to propose any mechanism of balance control on the basis of high threshold peripheral mechanisms. For example, some authors have proposed an intermittent control process as a solution to low resolution afferent signals (Bottaro *et al.*, 2008). Our data in chapter 3, where we found a high resolution afferent response to a small perturbation, do not support this notion. Secondly, we propose that reflexes do play some stabilising role in quiet standing, the extent to which is yet to be fully determined. We do not doubt that there is a wealth of evidence that reflexes are not the only story (Lakie *et al.*, 2003; Loram *et al.*, 2005*b*, 2005*c*, 2006*a*; Lakie & Loram, 2006), but we cannot be persuaded that they are entirely irrelevant.

Many researchers appear to understand balance in one of two ways: reflex control (Van der Kooij & De Vlugt, 2007; Deliagina *et al.*, 2007; Lockhart & Ting, 2007; Welch & Ting, 2008; Mergner, 2010), or higher level control (Loram *et al.*, 2005*c*, 2007*b*, 2009*d*, 2009*c*). In the third experimental chapter of this thesis, we conducted an experiment to try and integrate both of these ideas. We asked subjects to balance an inverted pendulum either using their ankle musculature, or by using their forearm muscles. In both cases all sensory feedback was provided through proprioceptive afferents via ankle rotation. In the condition where subjects controlled with their legs, both reflex and higher level pathways were available. In contrast, when controlling with their arms, they were engaging in a purely higher level manual control task in a similar vein to that which has been studied previously (Lakie *et al.*,

2003; Lakie & Loram, 2006; Loram *et al.*, 2009*a*). Additionally, we altered the 'proprioceptive gain' in the task by changing the gain between inverted pendulum angle and ankle rotation. We reasoned that higher proprioceptive gain would encourage proportionally more reflex control because afferent input signals would be larger whereas lower proprioceptive gain might encourage a greater proportion of voluntary control because afferent input signals would be smaller. This enabled us to compare one condition, where we expected an increasing reflex contribution with increased proprioceptive gain, with another condition where we expected no reflex contribution regardless of proprioceptive gain. A comparison of both modes of control revealed that, at artificially high gains, control using the legs was proportionately superior to control using the arm. However, at artificially low gains, performance between the two modes of control was indistinguishable. We attributed this difference to reflexes that become more prominent with larger faster ankle rotations at higher proprioceptive gains. A simple model was then used to demonstrate the viability of this explanation.

These experiments suggested that reflexes confer an advantage to balance control at artificially high gains in a task that is known to be similar to normal quiet standing (Fitzpatrick *et al.*, 1992; Fitzpatrick & McCloskey, 1994; Loram *et al.*, 2001; Loram & Lakie, 2002*a*). Although we manipulated the sensory gain in this study, we did not apply a perturbation: all our observations are drawn from an undisturbed closed loop system. This is crucial because perturbation studies can always be criticised on the grounds that they distort the system to which they are applied (Loram *et al.*, 2005*a*). When the data from this experiment are coupled with the evidence of high sensitivity reflex control discussed above, it is logical to propose that reflex control was also present in the physiological and even

lower sensory gain conditions. If reflex control operates at a constant low gain that is approximately proportional to ankle rotation size and speed, its contribution will be particularly small at low proprioceptive gains. Indeed, our theoretical model showed that the presence of reflex control may be masked by more dominant higher level loops when sensory gain is low (or when ankle rotations are small).

What could be the purpose of such low gain reflex control? A low gain continuously acting reflex mechanism may serve to increase the time constant of the human 'inverted pendulum' (Loram & Lakie, 2002*b*; Loram *et al.*, 2007*a*). It has previously been demonstrated that manual hand balancing of an inverted pendulum becomes increasingly difficult as the time constant of the load decreases (Lakie *et al.*, 2003; Loram *et al.*, 2006*a*). Even a small neural reflex contribution in combination with passive ankle stiffness could reduce the burden on a higher level more complex control process. In support of this hypothesis, we note the increased coherence between disturbance and response in a manual balancing task when the load stability was increased by only 15 percent (from 85 % stable to 100 % stable) (Loram *et al.*, 2009*a*). This means that participants were able nullify the effects of a random disturbance more effectively when the time constant of the load was increased by a relatively small margin. Thus, even small changes in stability could confer an advantage to more computationally intensive higher level control that is subject to longer time delays.

The strongest evidence for the presence of higher level control in human standing balance is derived from the striking similarities between manual balance control and quiet standing balance control. When balancing an unstable inverted pendulum by hand through a compliant linkage, a paradigm mechanically analogous to the calf muscles pulling on a

compliant achilles tendon to balance the human inverted pendulum, subjects characteristically make two to three pulsatile control adjustments per second (Lakie *et al.*, 2003). This is very similar to the rate of fluctuations in calf muscle length observed during quiet standing (Loram *et al.*, 2005*c*). Further experiments have corroborated these findings (Loram *et al.*, 2005*b*, 2006*a*, 2010, 2012; Lakie & Loram, 2006) and the result remains either a remarkable coincidence, or an indication of the presence of higher level control in human balance control.

There are a number of reasons why an intermittent pulsatile control strategy may confer some advantages over more traditional continuous feedback controllers. Firstly, intermittent controllers are more robust in the face of long time delays (Gawthrop *et al.*, 2011). When a continuous feedback controller is used to stabilise an inverted pendulum, stability is threatened by long time delays. This is because it can be highly inappropriate to constantly correct for errors that happened in the past. This can result in wild oscillation and loss of balance. Intermittent control is not continuous and is consequently less prone to such problems. This is a potentially useful feature in biological systems where substantial time delays are common. Secondly, there may be some increase in the quality of feedback that is available when adopting a pulsatile control strategy (Loram *et al.*, 2010). When correcting continuously in proportion to sensory feedback, it is difficult to distinguish between the effect of corrective actions and the effect of other forces acting on the load. Controlling in a pulsatile manner means there are more distinct periods of action separated by periods of non-action. During periods of non-action sensory feedback is not corrupted by motor noise which may allow for better understanding of load dynamics and external disturbances. In our fourth experimental chapter we hypothesised that intermittent control

tends to proceed as alternations between action and sensation, and that this alternation permits periods of higher quality sensation than would not be available otherwise. We reasoned that, if control is broadly alternating between action and sensation then the quality of feedback should not be static but should change depending on its temporal proximity to motor actions.

We studied intermittent human visuo-manual balance control and used visual occlusions to block all sensory feedback for brief periods. Our key findings were that sensory information was not equally useful at all times, but varied depending on its temporal relationship to each control output. Specifically, for a brief period after each motor output, sensory information could be blocked with minimal impact on either task performance, or the rate at which corrective actions were made. This led us to speculate that control was indeed alternating between actions and sensation. Biologically this idea may be relevant because it is well known that sensation is attenuated during active movement (Collins *et al.*, 1998; Seki *et al.*, 2003), and serial pulsatile control presents a viable strategy to deal with this. This is a plausible rationale for adopting an intermittent control strategy in a task such as quiet standing and these ideas require further investigation.

Limitations and future directions

For clarity, we discuss limitations and future experiments in relation to each chapter individually. We omit the first experimental chapter from this section because it is a simple descriptive methods validation study that requires minimal interpretation.

<u>Experimental chapter 2</u>

Use of single perturbation

In these experiments we used a single low velocity platform tilt to reveal a high sensitivity neural control process in human standing. In an ideal experiment, we would have collected substantially more data on a variety of different velocity ramps and attempted to define position/velocity and acceleration thresholds. In reality, this sort of experiment is difficult. Our experiment required a large amount of averaging to reveal a small response buried in large background noise. The analysis of ultrasound videos, even with our newly developed technique, is time consuming. Thus, to repeat the experiment using a variety of perturbations would require a large effort for a relatively minor advance in understanding.

Nature of perturbation

We used a simple position ramp to produce the support surface rotation as in Gurfinkel *et al.*, (1995). A position ramp is equal to a velocity step which means that the acceleration can be quite high at the onset of the perturbation. Other researchers have minimised the initial acceleration by using 'raised cosine' velocity profiles (Loram & Lakie, 2002*b*; Maurer *et al.*, 2006*b*). This raises an interesting point as to whether we would have observed a neural response given a smaller initial acceleration. We do not know the answer to this question, and, as we mentioned above it may be worth further investigation but we consider that the perturbation we used was sufficiently small (in position velocity and acceleration) to justify our interpretation of high sensitivity control.

Different types of perturbation

It would be informative to use different types of perturbation to stimulate different sensory modalities. For example, a torque perturbation at the waist could be used to pull subjects forward. In this case we stimulate proprioceptive afferents via an ankle rotation, and

vestibular afferents through the body lean. Vision could also be included/excluded. It should be possible to study the early response of each sensory modality in isolation, and to study the responses in combination. This may enable the temporal decomposition of the contribution of each sensory modality to the normal fully functioning response. However, we note that the exclusion of any sensory modality will create a sensory conflict. If, for example, a moving room is used to perturb the visual system alone, there will be no direct activation of proprioceptive or vestibular sensory systems. It is difficult to know whether such a false sensory signal will reproduce a normal visually mediated response.

Experimental chapter 3

Lack of perturbation

One limitation of this study is that we did not use a perturbation. Using a continuous random perturbation would have permitted more substantive analysis. We could have calculated transfer functions which would have revealed the feedback time delay and frequency response of each condition (leg control or arm control). These data would have allowed a more concrete interpretation of the biological pathways involved in each condition. While we consider this to be valid criticism of the experiment, we also think there are advantages in unperturbed experiments. Perturbations studies can always be criticised for changing the nature of a task such that the controller response may not apply in the unperturbed context. Additionally, in our experiments, where we manipulated sensory gain, adding a perturbation may have rendered some conditions insurmountably difficult for the subject to perform. However, we concede that repeating the experiment (with some difficult conditions omitted) with the inclusion of a multi-sine before load disturbance (as

we used in our fourth experimental chapter) would be highly illuminating and provide an excellent companion study to the one presented in this thesis.

Problems with equivalent tasks

It is always a valid criticism that 'equivalent tasks' such as inverted pendulum balancing do not adequately recreate the conditions of real quiet standing. We do not think this means that such experiments are meaningless but we acknowledge it is important to be cautious in interpretation. It is possible that voluntary control is more prominent in novel tasks. Even with substantial practice and training, it is impossible to replicate the level of familiarity associated with years of normal quiet standing. It becomes very difficult to know what influence such levels of familiarity have on the properties of control. Sometimes the equivalent task can be conceptually and technically impressive, and it is true that some experiments would be impossible without these paradigms. However, in future studies we would urge that the rigorous reductionist approach is complimented by experimental designs that are more ecologically valid.

Experiment 4

Do our findings generalise to sustained joystick control?

We asked subjects to balance a virtual inverted pendulum through gentle taps of a joystick. An important question is whether our findings would generalise to sustained (continuous contact) joystick control. This question is echoed in a previous study (Loram *et al.*, 2010). At present, there is no way of definitively answering this question. The advantage of control by gentle taps is that each control action is clearly defined. This makes it possible to link a visual occlusion precisely with each motor output (each tap). Identification of discrete

motor outputs during sustained control is methodologically difficult, particularly in real time. It may be possible to develop techniques that trigger off a range of variables such as muscle length changes (using ultrasound) or EMG. If it were possible to do so, repeating this experiment with a sustained control paradigm would have a high impact on the motor control field.

Identification of precise duration of period of sensory redundancy

In these experiments we estimated that the first 125 ms of sensory information following each control action was largely redundant. We experimentally demonstrated that blocking this period of sensation with a visual occlusion made no statistical difference to performance and had no impact on the rate of correction actions. We do not suggest that sensory information is not available during this period, but that sensory information is not used during this time. However, further experiments could use this paradigm to more precisely identify the period of sensory redundancy that immediately follows each control action. This would require different conditions where the length of the visual occlusion was varied.

Control of zero and first order loads

In all experiments we asked subjects to balance second order loads. We changed the time constant of the loads but we did not change load order. The advantage of using a second order load is that it is most analogous to real human standing because the standing human body approximates a simple second order load (inverted pendulum). The disadvantage is that we do not know whether our findings would generalise to control of zero or first order

loads. Future experiments could determine whether sensory feedback was similarly depressed following each motor action when controlling zero and first order loads.

General conclusions

We are now in a position to arrive at some simple general conclusions. We propose that the control of quiet standing is achieved through parallel control loops. Reflex control operates at a low gain probably with relatively small delays, and is a useful mechanism for increasing the time constant of the human inverted pendulum. This facilitates the operation of a higher level control system that is more computationally intensive and is subject to longer time delays. We favour the idea that this takes the form of intermittent serial ballistic control. This paradigm was originally postulated by Craik to explain human manual control (Craik, 1947, 1948; Vince, 1948) but a large body of evidence now suggests it is an entirely plausible explanation for quiet standing control (Loram & Lakie, 2002*a*; Lakie *et al.*, 2003; Loram *et al.*, 2005*b*, 2005*c*, 2006*a*, 2009*a*, 2010, 2012; Lakie & Loram, 2006; Gawthrop *et al.*, 2009). We speculate that this mechanism operates in alternating epochs of action and sensation in order to deal with the attenuation in sensation that occurs during active movements (Collins *et al.*, 1998; Seki *et al.*, 2003; Voss *et al.*, 2008), and to allow for higher quality sensory feedback.

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